

indole and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 497.0 ( $M + H$ )<sup>+</sup>.

#### Example 522

5 **N-[3-(1-{[7-(4-ACETYLPHENYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure D and Scheme N using 1-[4-(1H-indol-7-yl)phenyl]ethanone and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 493.6 ( $M + H$ )<sup>+</sup>.

10

#### Example 523

**N-[3-(1-{[6-(4-ETHYLPHENYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure D and Scheme N using 6-(4-ethylphenyl)-1H-indole and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 480.1 ( $M + H$ )<sup>+</sup>.

15

#### Example 524

**2-METHYL-N-[3-(1-{[7-(2-METHYLPHENYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE:** Prepared by Procedure D and Scheme N using 7-(2-methylphenyl)-1H-indole and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 466.1 ( $M + H$ )<sup>+</sup>.

20

#### Example 525

**N-[3-(1-{[6-(2-FLUOROPHENYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure D and Scheme N using 6-(2-fluorophenyl)-1H-indole and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 470.2 ( $M + H$ )<sup>+</sup>.

**5-(4-METHYLPHENOXY)-1H-INDOLE:** Prepared by Procedure J and Scheme U using 5-bromo-1H-indole and p-cresol: ESMS  $m/e$ : 224.0 ( $M + H$ )<sup>+</sup>.

30

**Example 526**

**N-(3-{1-[(5-BROMO-1H-INDOL-3-YL)METHYL]-4-**

**PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by

5 Procedure D and Scheme N using 5-bromo-1H-indole and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS m/e: 454.0 (M + H)<sup>+</sup>.

**1-(4-PYRIDINYL)-6-(TRIFLUOROMETHYL)-1H-INDOLE:** Prepared

10 by Procedure C and Scheme O using 6-(trifluoromethyl)-1H-indole and 4-iodopyridine: ESMS m/e: 262.9 (M + H)<sup>+</sup>.

**Example 527**

**2-METHYL-N-[3-(1-{[5-(4-METHYLPHENOXY)-1H-INDOL-3-**

15 **YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE:** Prepared by Procedure D and Scheme N using 5-(4-methylphenoxy)-1H-indole and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS m/e: 481.9 (M + H)<sup>+</sup>.

20 **1-(4-METHYLPHENYL)-1H-INDOLE:** Prepared by Procedure C and Scheme O using 1H-indole and 1-iodo-4-methylbenzene: ESMS m/e: 208.0 (M + H)<sup>+</sup>.

25 **1-(3-METHYLPHENYL)-1H-INDOLE:** Prepared by Procedure C and Scheme O using 1H-indole and 1-iodo-3-methylbenzene: ESMS m/e: 208.0 (M + H)<sup>+</sup>.

30 **1-[3-(TRIFLUOROMETHYL)PHENYL]-1H-INDOLE:** Prepared by Procedure C and Scheme O using 1H-indole and 1-iodo-3-(trifluoromethyl)benzene: ESMS m/e: 262.0 (M + H)<sup>+</sup>.

**1-(4-METHOXYPHENYL)-1H-INDOLE:** Prepared by Procedure C and Scheme O using 1H-indole and 1-iodo-4-methoxybenzene: ESMS  $m/e$ : 224.0 (M + H)<sup>+</sup>.

5 **1-(2-METHOXYPHENYL)-1H-INDOLE:** Prepared by Procedure C and Scheme O using 1H-indole and 1-iodo-2-methoxybenzene: ESMS  $m/e$ : 224.0 (M + H)<sup>+</sup>.

10 **1-(3-METHOXYPHENYL)-1H-INDOLE:** Prepared by Procedure C and Scheme O using 1H-indole and 1-iodo-3-methoxybenzene: ESMS  $m/e$ : 224.0 (M + H)<sup>+</sup>.

15 **1-(2-METHYLPHENYL)-1H-INDOLE:** Prepared by Procedure C and Scheme O using 1H-indole and 1-iodo-2-methylbenzene: ESMS  $m/e$ : 208.0 (M + H)<sup>+</sup>.

20 **6-FLUORO-1-PHENYL-1H-INDOLE:** Prepared by Procedure C and Scheme O using 6-fluoro-1H-indole and iodobenzene: ESMS  $m/e$ : 212.0 (M + H)<sup>+</sup>.

**6-CHLORO-1-PHENYL-1H-INDOLE:** Prepared by Procedure C and Scheme O using 6-chloro-1H-indole and iodobenzene: ESMS  $m/e$ : 228.0 (M + H)<sup>+</sup>.

25 **7-CHLORO-1-PHENYL-1H-INDOLE:** Prepared by Procedure C and Scheme O using 7-chloro-1H-indole and iodobenzene: ESMS  $m/e$ : 228.0 (M + H)<sup>+</sup>.

30 **6-(2-FLUOROPHENYL)-1H-INDOLE:** Prepared by Procedure I and Scheme T using 6-bromo-1H-indole and 2-fluorophenylboronic acid: ESMS  $m/e$ : 211.9 (M + H)<sup>+</sup>.

**Example 528**

**2-METHYL-N-{3-[1-(7-OXO-7-PHENYLHEPTYL)-4-**

**PIPERIDINYL]PHENYL}PROPANAMIDE:** Prepared by Procedure K  
and Scheme B1 using 7-chloro-1-phenyl-1-heptanone and 2-  
5 methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*:  
435.1 (M + H)<sup>+</sup>.

**Example 529**

**2-METHYL-N-{3-[1-(6-OXO-6-PHENYLHEXYL)-4-**

10 **PIPERIDINYL]PHENYL}PROPANAMIDE:** Prepared by Procedure K  
and Scheme B1 using 6-chloro-1-phenyl-1-hexanone and 2-  
methyl-N-[3-(4-piperidinyl)phenyl]propanamide: Anal.  
Calcd for C<sub>27</sub>H<sub>36</sub>N<sub>2</sub>O<sub>2</sub>+0.1CHCl<sub>3</sub>: C, 75.3; H, 8.39; N, 6.46.  
Found: C, 75.4; H, 7.89; N, 6.18; ESMS *m/e*: 421.1 (M +  
15 H)<sup>+</sup>.

**Example 530**

**2-METHYL-N-{3-[1-(5-OXO-5-PHENYLPENTYL)-4-**

20 **PIPERIDINYL]PHENYL}PROPANAMIDE:** Prepared by Procedure K  
and Scheme B1 using 5-chloro-1-phenyl-1-pentanone and 2-  
methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*:  
407.1 (M + H)<sup>+</sup>.

**Example 531**

25 **N-(3-{1-[4-(4-METHOXYPHENYL)-4-OXOBUTYL]-4-**

**PIPERIDINYL}PHENYL)PROPANAMIDE:** Prepared by Procedure K  
and Scheme B1 using 4-chloro-1-(4-methoxyphenyl)-1-  
butanone and N-[3-(4-piperidinyl)phenyl]propanamide:  
ESMS *m/e*: 409.2 (M + H)<sup>+</sup>.

**Example 532**

30 **N-(3-{1-[4-(4-CHLOROPHENYL)-4-OXOBUTYL]-4-**

**PIPERIDINYL}PHENYL)PROPANAMIDE:** Prepared by Procedure K  
and Scheme B1 using 4-chloro-1-(4-chlorophenyl)-1-

butanone and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 413.1 (*M* + *H*)<sup>+</sup>.

**Example 533**

5 *N*-(3-{1-[4-(4-BROMOPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure K and Scheme B1 using 1-(4-bromophenyl)-4-chloro-1-butanone and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 457.1 (*M* + *H*)<sup>+</sup>.

10

**Example 534**

*N*-(3-{1-[4-(4-TERT-BUTYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure K and Scheme B1 using 1-(4-tert-butylphenyl)-4-chloro-1-butanone and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 435.2 (*M* + *H*)<sup>+</sup>.

15

**Example 535**

*N*-(3-{1-[4-(4-FLUOROPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure K and Scheme B1 using 4-chloro-1-(4-fluorophenyl)-1-butanone and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 397.2 (*M* + *H*)<sup>+</sup>.

20

**Example 536**

*N*-(3-{1-[4-OXO-4-(4-PHENOXYPHENYL)BUTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure K and Scheme B1 using 4-chloro-1-(4-phenoxyphenyl)-1-butanone and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 471.2 (*M* + *H*)<sup>+</sup>.

25

30

**Example 537**

***N*-(3-{1-[4-(4-ISOPROPYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL) CYCLOPROPANECARBOXAMIDE:**

Prepared by Procedure K and Scheme B1 using 4-chloro-1-(4-isopropylphenyl)-1-butanone and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 433.2 (*M* + *H*)<sup>+</sup>.

**Example 538**

***N*-(3-{1-[4-(4-METHOXYPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL) CYCLOPROPANECARBOXAMIDE:**

Prepared by Procedure K and Scheme B1 using 4-chloro-1-(4-methoxyphenyl)-1-butanone and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 421.2 (*M* + *H*)<sup>+</sup>.

**Example 539**

***N*-(3-{1-[4-OXO-4-(4-PHENOXYPHENYL) BUTYL]-4-PIPERIDINYL}PHENYL) CYCLOPROPANECARBOXAMIDE:**

Prepared by Procedure K and Scheme B1 using 4-chloro-1-(4-phenoxyphenyl)-1-butanone and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 483.2 (*M* + *H*)<sup>+</sup>.

**Example 540**

***N*-(3-{1-[4-(4-ISOPROPYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL) PROPANAMIDE:**

Prepared by Procedure K and Scheme B1 using 4-chloro-1-(4-isopropylphenyl)-1-butanone and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 421.3 (*M* + *H*)<sup>+</sup>.

**Example 541**

***N*-(3-{1-[4-(4-*TERT*-BUTYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL) CYCLOPROPANECARBOXAMIDE:** Prepared by Procedure K and Scheme B1 using 1-(4-*tert*-butylphenyl)-4-chloro-1-butanone and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 447.2 (*M* + *H*)<sup>+</sup>.

**Example 542**

***N*-(3-{1-[4-(4-METHYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL) PROPANAMIDE:** Prepared by Procedure K and Scheme B1 using 4-chloro-1-(4-methylphenyl)-1-butanone and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 393.2 (*M* + *H*)<sup>+</sup>.

**Example 543**

***N*-(3-{1-[4-(3,4-DIMETHYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL) PROPANAMIDE:** Prepared by Procedure K and Scheme B1 using 4-chloro-1-(3,4-dimethylphenyl)-1-butanone and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 407.2 (*M* + *H*)<sup>+</sup>.

**Example 544**

***N*-(3-{1-[4-(4-BROMOPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL) CYCLOPROPANECARBOXAMIDE:** Prepared by Procedure K and Scheme B1 using 1-(4-bromophenyl)-4-chloro-1-butanone and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 469.1 (*M* + *H*)<sup>+</sup>.

**Example 545**

***N*-(3-{1-[5-(4-FLUOROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL) PROPANAMIDE:** Prepared by Procedure K and Scheme B1 using 5-chloro-1-(4-fluorophenyl)-1-

pentanone and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 411.2 (*M* + *H*)<sup>+</sup>.

#### Example 546

5 *N*-(3-{1-[4-(3,4-DIMETHYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL) CYCLOPROPANECARBOXAMIDE: Prepared by Procedure K and Scheme B1 using 4-chloro-1-(3,4-dimethylphenyl)-1-butanone and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*:  
10 419.2 (*M* + *H*)<sup>+</sup>.

#### Example 547

*N*-(3-{1-[4-(4-METHYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL) CYCLOPROPANECARBOXAMIDE: Prepared by  
15 Procedure K and Scheme B1 using 4-chloro-1-(4-methylphenyl)-1-butanone and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*:  
405.2 (*M* + *H*)<sup>+</sup>.

#### 20 Example 548

*N*-(3-{1-[4-(4-FLUOROPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL) CYCLOPROPANECARBOXAMIDE: Prepared by  
Procedure K and Scheme B1 using 4-chloro-1-(4-fluorophenyl)-1-butanone and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*:  
25 409.2 (*M* + *H*)<sup>+</sup>.

#### Example 549

*N*-(3-{1-[5-(3-FLUOROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL) CYCLOPROPANECARBOXAMIDE: Prepared by  
30 Procedure K and Scheme B1 using 5-chloro-1-(3-fluorophenyl)-1-pentanone and *N*-[3-(4-



piperidinyl)phenyl]cyclopropanecarboxamide: ESMS  $m/e$ :  
423.2 (M + H)<sup>+</sup>.

#### Example 550

5 **N-[3-(1-{5-oxo-5-[4-(trifluoromethyl)phenyl]pentyl}-4-piperidinyl)phenyl]propanamide:** Prepared by Procedure K and Scheme B1 using 5-chloro-1-[4-(trifluoromethyl)phenyl]-1-pentanone and N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 461.2 (M + H)<sup>+</sup>.

10

#### Example 551

**N-(3-{1-[5-(4-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)cyclopropanecarboxamide:** Prepared by Procedure K and Scheme B1 using 5-chloro-1-(4-fluorophenyl)-1-pentanone and N-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS  $m/e$ : 423.2 (M + H)<sup>+</sup>.

15

#### Example 552

20 **N-(3-{1-[5-(3-nitrophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)propanamide:** Prepared by Procedure K and Scheme B1 using 5-chloro-1-(3-nitrophenyl)-1-pentanone and N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 438.2 (M + H)<sup>+</sup>.

25

#### Example 553

**N-(3-{1-[5-(3-nitrophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)cyclopropanecarboxamide:** Prepared by Procedure K and Scheme B1 using 5-chloro-1-(3-nitrophenyl)-1-pentanone and N-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS  $m/e$ : 450.2 (M + H)<sup>+</sup>.

30

**Example 554**

***N*-(3-{1-[5-(2-FLUOROPHENYL)-5-OXOPENTYL]-4-**

**PIPERIDINYL}PHENYL)PROPANAMIDE:** Prepared by Procedure K  
and Scheme B1 using 5-chloro-1-(2-fluorophenyl)-1-  
5 pentanone and *N*-[3-(4-piperidinyl)phenyl]propanamide:  
ESMS *m/e*: 411.2 (*M* + *H*)<sup>+</sup>.

**Example 555**

***N*-(3-{1-[5-(3-FLUOROPHENYL)-5-OXOPENTYL]-4-**

**PIPERIDINYL}PHENYL)PROPANAMIDE:** Prepared by Procedure K  
10 and Scheme B1 using 5-chloro-1-(3-fluorophenyl)-1-  
pentanone and *N*-[3-(4-piperidinyl)phenyl]propanamide:  
ESMS *m/e*: 411.2 (*M* + *H*)<sup>+</sup>.

**Example 556**

***N*-(3-{1-[5-(4-NITROPHENYL)-5-OXOPENTYL]-4-**

**PIPERIDINYL}PHENYL)PROPANAMIDE:** Prepared by Procedure K  
and Scheme B1 using 5-chloro-1-(4-nitrophenyl)-1-  
pentanone and *N*-[3-(4-piperidinyl)phenyl]propanamide:  
20 ESMS *m/e*: 438.1 (*M* + *H*)<sup>+</sup>.

**Example 557**

***N*-(3-{1-[5-(4-NITROPHENYL)-5-OXOPENTYL]-4-**

**PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE:** Prepared by  
25 Procedure K and Scheme B1 using 5-chloro-1-(4-  
nitrophenyl)-1-pentanone and *N*-[3-(4-  
piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*:  
450.1 (*M* + *H*)<sup>+</sup>.

**Example 558**

***N*-(3-{1-[5-(4-CHLOROPHENYL)-5-OXOPENTYL]-4-**

**PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE:** Prepared by  
30 Procedure K and Scheme B1 using 5-chloro-1-(4-

chlorophenyl)-1-pentanone and N-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS m/e: 439.1 (M + H)<sup>+</sup>.

5

**Example 559**

N-[3-(1-{5-oxo-5-[2-(trifluoromethyl)phenyl]pentyl}-4-piperidinyl)phenyl]propanamide: Prepared by Procedure K and Scheme B1 using 5-chloro-1-[2-(trifluoromethyl)phenyl]-1-pentanone and N-[3-(4-piperidinyl)phenyl]propanamide: ESMS m/e: 461.2 (M + H)<sup>+</sup>.

10

**Example 560**

N-[3-(1-{5-oxo-5-[2-(trifluoromethyl)phenyl]pentyl}-4-piperidinyl)phenyl]cyclopropanecarboxamide: Prepared by Procedure K and Scheme B1 using 5-chloro-1-[2-(trifluoromethyl)phenyl]-1-pentanone and N-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS m/e: 473.2 (M + H)<sup>+</sup>.

15

20

**Example 561**

N-(3-{1-[5-(4-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)propanamide: Prepared by Procedure K and Scheme B1 using 5-chloro-1-(4-chlorophenyl)-1-pentanone and N-[3-(4-piperidinyl)phenyl]propanamide: ESMS m/e: 427.1 (M + H)<sup>+</sup>.

25

**Example 562**

N-(3-{1-[5-(3-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)propanamide: Prepared by Procedure K and Scheme B1 using 5-chloro-1-(3-chlorophenyl)-1-pentanone and N-[3-(4-piperidinyl)phenyl]propanamide: ESMS m/e: 427.1 (M + H)<sup>+</sup>.

30

**Example 563**

**N-(3-{1-[5-(2-FLUOROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL) CYCLOPROPANECARBOXAMIDE:** Prepared by Procedure K and Scheme B1 using 5-chloro-1-(2-fluorophenyl)-1-pentanone and N-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 423.1 (M + H)<sup>+</sup>.

**Example 564**

**N-(3-{1-[5-(3-CHLOROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL) CYCLOPROPANECARBOXAMIDE:** Prepared by Procedure K and Scheme B1 using 5-chloro-1-(3-chlorophenyl)-1-pentanone and N-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 439.1 (M + H)<sup>+</sup>.

**Example 565**

**N-[3-(1-{5-EXO-5-[4-(TRIFLUOROMETHYL)PHENYL]PENTYL]-4-PIPERIDINYL}PHENYL) CYCLOPROPANECARBOXAMIDE:** Prepared by Procedure K and Scheme B1 using 5-chloro-1-[4-(trifluoromethyl)phenyl]-1-pentanone and N-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 473.2 (M + H)<sup>+</sup>.

**Example 566**

**N-(3-{1-[5-(2-CHLOROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL) PROPANAMIDE:** Prepared by Procedure K and Scheme B1 using 5-chloro-1-(2-chlorophenyl)-1-pentanone and N-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 427.1 (M + H)<sup>+</sup>.

**Example 567**

***N*-(3-{1-[5-(2-CHLOROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE:**

Prepared by Procedure K and Scheme B1 using 5-chloro-1-(2-chlorophenyl)-1-pentanone and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 439.1 (*M* + *H*)<sup>+</sup>.

**Example 568**

***N*-[3-(1-{5-EXO-5-[3-(TRIFLUOROMETHYL)PHENYL]PENTYL]-4-PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE:**

Prepared by Procedure K and Scheme B1 using 5-chloro-1-[3-(trifluoromethyl)phenyl]-1-pentanone and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 473.2 (*M* + *H*)<sup>+</sup>.

**Example 569**

***N*-(3-{1-[4-(3,4-DIMETHYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)-*N*,2-DIMETHYLPROPANAMIDE:**

Prepared by Procedure T and Scheme AD using *N*-(3-{1-[4-(3,4-dimethylphenyl)-4-oxobutyl]-4-piperidinyl}phenyl)-2-methylpropanamide and methyl iodide: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.76 (s, 1H), 7.72 (dd, 1H, *J* = 1.8, 7.7 Hz), 7.33 (t, 1H, *J* = 8.8 Hz), 7.22 (d, 1H, *J* = 7.8 Hz), 7.18 (d, 1H, *J* = 8.8 Hz), 7.01 (m, 2H), 3.24 (s, 3H), 3.10 (d, 1H, *J* = 10.6 Hz), 3.00 (t, 1H, *J* = 7.6 Hz), 2.49 (m, 4H), 2.33 (s, 6H), 2.11 (m, 3H), 1.99 (m, 1H), 1.79 (m, 4H), 1.26 (t, 2H, *J* = 7.6 Hz), 1.02 (d, 6H, *J* = 7.6 Hz); ESMS *m/e*: 435.2 (*M* + *H*)<sup>+</sup>.

**Example 570**

**2-METHYL-*N*-(3-[1-(1-METHYL-4-OXO-4-PHENYLBUTYL)-4-PIPERIDINYL]PHENYL)PROPANAMIDE:**

Prepared by Procedure K

and Scheme B1 using 4-chloro-1-phenyl-1-pentanone and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 407.2 ( $M + H$ )<sup>+</sup>.

5

**Example 571**

N-[3-(1-{5-oxo-5-[3-(trifluoromethyl)phenyl]pentyl}-4-piperidinyl)phenyl]propanamide: Prepared by Procedure K and Scheme B1 using 5-chloro-1-[3-(trifluoromethyl)phenyl]-1-pentanone and N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 461.2 ( $M + H$ )<sup>+</sup>.

10

3-(5-chloropentanoyl)-4-(3,4-difluorophenyl)-1,3-oxazolidin-2-one: Prepared by Procedure AF and Scheme H using 4-(3,4-difluorophenyl)-1,3-oxazolidin-2-one and 5-chloropentanoyl chloride.

15

3-(5-chloropentyl)-4-(3,4-difluorophenyl)-1,3-oxazolidin-2-one: Prepared by Procedure G and Scheme C1 using 4-(3,4-difluorophenyl)-1,3-oxazolidin-2-one and 1-bromo-5-chloropentane.

20

**Example 572**

N-[3-(1-{5-[(4R)-4-(3,4-difluorophenyl)-2-oxo-1,3-oxazolidin-3-yl]-5-oxopentyl}-4-piperidinyl)phenyl]-2-methylpropanamide: Prepared by Procedure G and Scheme B1 using (4R)-3-(5-chloropentanoyl)-4-(3,4-difluorophenyl)-1,3-oxazolidin-2-one and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 528.2 ( $M + H$ )<sup>+</sup>.

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**Example 573**

(4R)-4-(3,4-difluorophenyl)-N-(3-{4-[3-(isobutyrylamino)phenyl]-1-piperidinyl}propyl)-2-oxo-

**1,3-OXAZOLIDINE-3-****CARBOXAMIDE:** Prepared by

Procedure AF and Scheme H using 4-nitrophenyl (4R)-4-(3,4-difluorophenyl)-2-oxo-1,3-oxazolidine-3-carboxylate and N-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-

5 methylpropanamide:  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.08 (t, 1H,  $J$  = 5.5 Hz), 7.45 (s, 2H), 7.38 (d, 1H,  $J$  = 8.6 Hz), 7.24-7.12 (m, 3H), 7.06 (m, 1H), 6.97 (d, 1H,  $J$  = 8.6 Hz), 5.40 (dd, 1H,  $J$  = 3.9, 8.8 Hz), 4.71 (t, 1H,  $J$  = 8.8 Hz), 4.23 (dd, 1H,  $J$  = 4.4, 9.1 Hz), 3.32 (qt, 2H,  $J$  = 6.1 Hz), 2.99 (d, 2H,  $J$  = 11.0 Hz), 2.49 (qt, 2H,  $J$  = 7.0 Hz), 2.41 (t, 2H,  $J$  = 7.0 Hz), 1.99 (m, 2H), 1.82-1.68 (m, 6H), 1.23 (d, 6H,  $J$  = 7.3 Hz); ESMS  $m/e$ : 529.1 ( $M + H$ ) $^+$ .

15 (4S)-3-(5-CHLOROPENTYL)-4-(3,4-DIFLUOROPHENYL)-1,3-OXAZOLIDIN-2-ONE: Prepared by Procedure G and Scheme C1 using (4S)-4-(3,4-difluorophenyl)-1,3-oxazolidin-2-one and 1-bromo-5-chloropentane.

20 *Example 574*

N-[3-(1-{5-[(4S)-4-(3,4-DIFLUOROPHENYL)-2-OXO-1,3-OXAZOLIDIN-3-YL]PENTYL}-4-PIPERIDINYL)PHENYL]-2-

25 METHYLPROPANAMIDE: Prepared by Procedure G and Scheme B1 using (4S)-3-(5-chloropentyl)-4-(3,4-difluorophenyl)-1,3-oxazolidin-2-one and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide:  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.48 (s, 1H), 7.32 (d, 1H,  $J$  = 8.6 Hz), 7.26-7.21 (m, 2H), 7.20-7.12 (m, 2H), 7.06 (m, 1H), 6.97 (d, 1H,  $J$  = 6.96 Hz), 4.76 (dd, 1H,  $J$  = 6.3, 8.3 Hz), 4.62 (t, 1H,  $J$  = 9.0 Hz), 4.06 (dd, 1H,  $J$  = 6.4, 8.7 Hz), 3.46 (m, 1H), 3.0 (d, 2H,  $J$  = 9.0 Hz), 2.77 (q, 1H,  $J$  = 6.8 Hz), 2.50 (q, 2H,  $J$  = 6.8 Hz), 2.31 (t, 2H,  $J$  = 6.8 Hz), 2.01 (m, 4H), 1.81 (m, 4H), 1.48 (m, 4H), 1.26 (d, 6H,  $J$  = 7.3

390  
Hz); Anal. Calcd for  $C_{28}H_{37}F_2N_3O_3 + HCl + 0.25CHCl_3$ :  
C, 60.6; H, 6.65; N, 7.25. Found: C, 60.7; H, 6.91; N,  
7.05; ESMS  $m/e$ : 514.2 (M + H)<sup>+</sup>.

#### Example 575

N-[3-(1-{5-[(4S)-4-(3,4-DIFLUOROPHENYL)-2-OXO-1,3-  
OXAZOLIDIN-3-YL]-5-OXOPENTYL}-4-PIPERIDINYL)PHENYL]-2-  
METHYLPROPANAMIDE: Prepared by Procedure G and Scheme  
B1 using (4S)-3-(5-chloropentanoyl)-4-(3,4-  
difluorophenyl)-1,3-oxazolidin-2-one and 2-methyl-N-[3-  
(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 528.1 (M +  
H)<sup>+</sup>.

#### Example 576

(4S)-4-(3,4-DIFLUOROPHENYL)-N-(3-{4-[3-  
(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}PROPYL)-2-OXO-  
1,3-OXAZOLIDINE-3-CARBOXAMIDE: Prepared by Procedure AF  
and Scheme H using 4-nitrophenyl (4S)-4-(3,4-  
difluorophenyl)-2-oxo-1,3-oxazolidine-3-carboxylate and  
N-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-  
methylpropanamide: ESMS  $m/e$ : 529.1 (M + H)<sup>+</sup>.

#### Example 577

(4S)-N-(3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-  
PIPERIDINYL}PROPYL)-2-OXO-4-(3,4,5-TRIFLUOROPHENYL)-1,3-  
OXAZOLIDINE-3-CARBOXAMIDE: Prepared by Procedure AF and  
Scheme H using 4-nitrophenyl (4S)-4-(3,4-  
difluorophenyl)-2-oxo-1,3-oxazolidine-3-carboxylate and  
N-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-  
methylpropanamide: ESMS  $m/e$ : 547.1 (M + H)<sup>+</sup>.

#### Example 578

(4S)-4-(3,5-DIFLUOROPHENYL)-N-(3-{4-[3-  
(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}PROPYL)-2-OXO-



**1,3-OXAZOLIDINE-3-****CARBOXAMIDE:** Prepared by

Procedure AF and Scheme H using 4-nitrophenyl (4S)-4-(3,4-difluorophenyl)-2-oxo-1,3-oxazolidine-3-carboxylate and N-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS  $m/e$ : 529.2 (M + H)<sup>+</sup>.

**Example 579****N-(3-{1-[3-(PHENYLSULFANYL) PROPYL]-4-**

**PIPERIDINYL}PHENYL) PROPANAMIDE:** Prepared by Procedure G and Scheme B1 using [(3-chloropropyl)sulfanyl]benzene and N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 382.9 (M + H)<sup>+</sup>.

**Example 580****N-(3-{1-[3-(PHENYLSULFANYL) PROPYL]-4-**

**PIPERIDINYL}PHENYL) CYCLOPROPANECARBOXAMIDE:** Prepared by Procedure G and Scheme B1 using [(3-chloropropyl)sulfanyl]benzene and N-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS  $m/e$ : 395.1 (M + H)<sup>+</sup>.

**Example 581****2-METHYL-N-(3-{1-[3-(PHENYLSULFANYL) PROPYL]-4-**

**PIPERIDINYL}PHENYL) PROPANAMIDE:** Prepared by Procedure G and Scheme B1 using [(3-chloropropyl)sulfanyl]benzene and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.63 (s, 1H), 7.48 (s, 1H), 7.33 (m, 3H), 7.27 (t, 2H, J = 7.5 Hz), 7.20 (t, 1H, J = 7.9 Hz), 7.15 (tt, 1H, J = 7.2, 1.4 Hz), 6.95 (d, 1H, J = 7.6 Hz), 2.97 (t, 4H, J = 7.3 Hz), 2.46 (m, 4H), 1.99 (dt, 2H, J = 11.4, 3.0 Hz), 1.84 (qt, 2H, J = 7.3 Hz), 1.77 (m, 4H), 1.21 (d, 6H, J = 6.8 Hz); ESMS  $m/e$ : 396.8 (M + H)<sup>+</sup>.

**Example 582**

***N*-(3-{1-[6-(PHENYLSULFANYL)HEXYL]-4-**

**PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE:** Prepared by  
 Procedure G and Scheme B1 using [(6-  
 5 chlorohexyl)sulfanyl]benzene and *N*-[3-(4-  
 piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*:  
 437.4 (*M* + *H*)<sup>+</sup>.

**Example 583**

***N*-(3-{1-[4-(PHENYLSULFANYL)BUTYL]-4-**

**PIPERIDINYL}PHENYL)PROPANAMIDE:** Prepared by Procedure G  
 and Scheme B1 using [(4-chlorobutyl)sulfanyl]benzene and  
*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 396.8  
 (*M* + *H*)<sup>+</sup>.

**Example 584**

***N*-(3-{1-[4-(PHENYLSULFANYL)BUTYL]-4-**

**PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE:** Prepared by  
 Procedure G and Scheme B1 using [(4-  
 20 chlorobutyl)sulfanyl]benzene and *N*-[3-(4-  
 piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*:  
 409.5 (*M* + *H*)<sup>+</sup>.

**Example 585**

**2-METHYL-*N*-(3-{1-[4-(PHENYLSULFANYL)BUTYL]-4-**

**PIPERIDINYL}PHENYL)PROPANAMIDE:** Prepared by Procedure G  
 and Scheme B1 using [(4-chlorobutyl)sulfanyl]benzene and  
 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS  
*m/e*: 410.6 (*M* + *H*)<sup>+</sup>.

**Example 586**

**2-METHYL-*N*-(3-{1-[5-(PHENYLSULFANYL)PENTYL]-4-**

**PIPERIDINYL}PHENYL)PROPANAMIDE:** Prepared by Procedure G

and Scheme B1 using [(5-chloropentyl)sulfanyl]benzene and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 425.1 (M + H)<sup>+</sup>.

5                   **Example 587**

**N-(3-{1-[5-(PHENYLSULFANYL)PENTYL]-4-PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE:** Prepared by Procedure G and Scheme B1 using [(5-chloropentyl)sulfanyl]benzene and N-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS  $m/e$ : 423.1 (M + H)<sup>+</sup>.

10

**[(6-CHLOROHEXYL)SULFANYL]BENZENE:** Prepared by Procedure R and Scheme Z using benzenethiol and 1-bromo-6-chlorohexane.

15

**[(4-CHLOROBUTYL)SULFANYL]BENZENE:** Prepared by Procedure R and Scheme Z using benzenethiol and 1-bromo-4-chlorobutane.

20

**Example 588**

**N-(3-{1-[6-(PHENYLSULFANYL)HEXYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE:** Prepared by Procedure G and Scheme B1 using [(6-chlorohexyl)sulfanyl]benzene and N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 425.4 (M + H)<sup>+</sup>.

25

**[(5-CHLOROPENTYL)SULFANYL]BENZENE:** Prepared by Procedure R and Scheme Z using benzenethiol and 1-bromo-5-chloropentane.

30

**[(3-CHLOROPROPYL)SULFANYL]BENZENE:** Prepared by Procedure R and Scheme Z using benzenethiol and 1-bromo-

3-chloropropane:  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.37-7.34 (m, 2H), 7.32-7.26 (m, 2H), 7.19 (tt, 1H,  $J = 1.4$ , 7.3 Hz), 3.67 (t, 2H,  $J = 6.6$  Hz), 3.08 (t, 2H,  $J = 6.6$  Hz), 2.06 (qt, 2H,  $J = 6.6$  Hz).

5

### Example 589

***N*-(3-{1-[5-(PHENYLSULFANYL)PENTYL]-4-**

**PIPERIDINYL}PHENYL)PROPANAMIDE:** Prepared by Procedure G and Scheme B1 using [(5-chloropentyl)sulfanyl]benzene and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 411.1 ( $M + H$ ) $^+$ .

10

**3-CHLOROPROPYL 4-FLUOROPHENYL SULFIDE:** Prepared by Procedure R and Scheme Z using 4-fluorobenzenethiol and 1-bromo-3-chloropropane.

15

**1-BROMO-2-[(3-CHLOROPROPYL)SULFANYL]BENZENE:** Prepared by Procedure R and Scheme Z using 2-bromobenzenethiol and 1-bromo-3-chloropropane.

20

**3-CHLOROPROPYL 4-FLUOROPHENYL SULFOXIDE:** Prepared by Procedure S and Scheme AA using 3-chloropropyl 4-fluorophenyl sulfide and 1 eq *m*-CPBA:  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.65-7.62 (m, 2H), 7.28-7.21 (m, 2H), 3.65 (m, 2H), 2.94 (m, 2H), 2.28 (m, 1H), 2.06 (m, 1H); ESMS  $m/e$ : 220.9 ( $M + H$ ) $^+$ .

25

**3-CHLOROPROPYL 3-FLUOROPHENYL SULFIDE:** Prepared by Procedure R and Scheme Z using 3-fluorobenzenethiol and 1-bromo-3-chloropropane.

30

**3-CHLOROPROPYL 2-FLUOROPHENYL SULFIDE:** Prepared by Procedure R and Scheme Z using 2-fluorobenzenethiol and 1-bromo-3-chloropropane.

1-BROMO-2-[(3-CHLOROPROPYL) SULFINYL] BENZENE: Prepared  
by Procedure S and Scheme AA using 1-bromo-2-[(3-  
chloropropyl)sulfanyl]benzene and 1 eq *m*-CPBA: ESMS *m/e*:  
5 282.8 (M + H)<sup>+</sup>.

1-CHLORO-2-[(3-CHLOROPROPYL) SULFANYL] BENZENE: Prepared  
by Procedure R and Scheme Z using 2-chlorobenzenethiol  
and 1-bromo-3-chloropropane.

10 1-CHLORO-3-[(3-CHLOROPROPYL) SULFANYL] BENZENE: Prepared  
by Procedure R and Scheme Z using 3-chlorobenzenethiol  
and 1-bromo-3-chloropropane.

15 1-CHLORO-4-[(3-CHLOROPROPYL) SULFANYL] BENZENE: Prepared  
by Procedure R and Scheme Z using 4-chlorobenzenethiol  
and 1-bromo-3-chloropropane.

20 1-BROMO-3-[(3-CHLOROPROPYL) SULFANYL] BENZENE: Prepared  
by Procedure R and Scheme Z using 3-bromobenzenethiol  
and 1-bromo-3-chloropropane.

25 1-BROMO-4-[(3-CHLOROPROPYL) SULFANYL] BENZENE: Prepared  
by Procedure R and Scheme Z using 4-bromobenzenethiol  
and 1-bromo-3-chloropropane.

3-CHLOROPROPYL 3,4-DIMETHYLPHENYL SULFIDE: Prepared by  
Procedure R and Scheme Z using 3,4-dimethylbenzenethiol  
and 1-bromo-3-chloropropane.

### 30 Example 590

*N*-[3-(1-{3-[(4-FLUOROPHENYL) SULFINYL] PROPYL}-4-  
PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE: Prepared by  
Procedure G and Scheme B1 using 3-chloropropyl 4-

fluorophenyl sulfoxide and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide:  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.64 (m, 2H), 7.53 (s, 1H), 7.24 (m, 5H), 6.94 (d, 1H,  $J = 7.7$  Hz), 2.89 (m, 4H), 2.45 (m, 4H), 1.99 (m, 3H), 1.77 (m, 5H), 1.24 (d, 6H,  $J = 6.8$  Hz); Anal. Calcd for  $\text{C}_{24}\text{H}_{31}\text{FN}_2\text{O}_2\text{S} + 0.6\text{EtOAc}$ : C, 65.5; H, 7.45; N, 5.79. Found: C, 65.4; H, 7.30; N, 5.73; ESMS  $m/e$ : 431.1 ( $\text{M} + \text{H}$ ) $^+$ .

#### Example 591

**N-[3-(1-{3-[(2-BROMOPHENYL) SULFINYL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure G and Scheme B1 using 1-bromo-2-[(3-chloropropyl)sulfinyl]benzene and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide: Anal. Calcd for  $\text{C}_{24}\text{H}_{31}\text{BrN}_2\text{O}_2\text{S} + 0.3\text{CHCl}_3$ : ESMS  $m/e$ : 491.0 ( $\text{M} + \text{H}$ ) $^+$ .

#### Example 592

**N-{3-[1-((3S)-3-{[(3,4-DIFLUOROPHENYL) SULFONYL] AMINO}-3-PHENYLPROPYL)-4-PIPERIDINYL] PHENYL}-2-METHYLPROPANAMIDE:** Prepared by Procedure Q1 and Scheme AC using 3,4-difluorobenzenesulfonyl chloride and N-(3-{1-[(3S)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS  $m/e$ : 556.2 ( $\text{M} + \text{H}$ ) $^+$ .

#### Example 593

**3-CHLORO-N-((1S)-3-{4-[3-(ISOBUTYRYLAMINO) PHENYL]-1-PIPERIDINYL}-1-PHENYLPROPYL)-2-THIOPHENECARBOXAMIDE:** Prepared by Procedure Q1 and Scheme AC using 3-chloro-2-thiophenecarbonyl chloride and N-(3-{1-[(3S)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS  $m/e$ : 524.2 ( $\text{M} + \text{H}$ ) $^+$ .

**Example 594**

***N*-(3-{1-[(3*S*)-3-({[5-(DIMETHYLAMINO)-1-NAPHTHYL] SULFONYL} AMINO)-3-PHENYLPROPYL]-4-PIPERIDINYL} PHENYL)-2-METHYLPROPANAMIDE:**

Prepared by Procedure Q1 and Scheme AC using 5-(dimethylamino)-1-naphthalenesulfonyl chloride and *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 613.3 (*M* + *H*)<sup>+</sup>.

**Example 595**

10 **2-METHYL-*N*-(3-[1-((3*S*)-3-{[(4-METHYLPHENYL) SULFONYL] AMINO}-3-PHENYLPROPYL)-4-PIPERIDINYL] PHENYL} PROPANAMIDE:** Prepared by Procedure Q1 and Scheme AC using 4-methylbenzenesulfonyl chloride and *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 534.2 (*M* + *H*)<sup>+</sup>.

**Example 596**

20 ***N*-(3-[1-((3*S*)-3-{[(3,5-DICHLORO-2-HYDROXYPHENYL) SULFONYL] AMINO}-3-PHENYLPROPYL)-4-PIPERIDINYL] PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure Q1 and Scheme AC using 3,5-dichloro-2-hydroxybenzenesulfonyl chloride and *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 605.4 (*M* + *H*)<sup>+</sup>.

**Example 597**

30 **2-METHYL-*N*-(3-(1-{(3*S*)-3-[(METHYLSULFONYL) AMINO]-3-PHENYLPROPYL}-4-PIPERIDINYL) PHENYL) PROPANAMIDE:** Prepared by Procedure Q1 and Scheme AC using methanesulfonyl chloride and *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 458.6 (*M* + *H*)<sup>+</sup>.

**Example 598**

***N*-{3-[1-((3*S*)-3-{[(4-FLUOROPHENYL) SULFONYL] AMINO}-3-PHENYLPROPYL)-4-PIPERIDINYL] PHENYL}-2-METHYLPROPANAMIDE:**

Prepared by Procedure Q1 and Scheme AC using 4-fluorobenzenesulfonyl chloride and *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 538.1 (*M* + *H*)<sup>+</sup>.

**Example 599**

***N*-{3-[1-((3*S*)-3-{[(4-*TERT*-BUTYLPHENYL) SULFONYL] AMINO}-3-PHENYLPROPYL)-4-PIPERIDINYL] PHENYL}-2-METHYLPROPANAMIDE:**

Prepared by Procedure Q1 and Scheme AC using 4-*tert*-butylbenzenesulfonyl chloride and *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 576.2 (*M* + *H*)<sup>+</sup>.

**Example 600**

***N*-{3-[1-((3*S*)-3-{[(2,5-DICHLOROPHENYL) SULFONYL] AMINO}-3-PHENYLPROPYL)-4-PIPERIDINYL] PHENYL}-2-METHYLPROPANAMIDE:**

Prepared by Procedure Q1 and Scheme AC using 2,5-dichlorobenzenesulfonyl chloride and *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 588.0 (*M* + *H*)<sup>+</sup>.

**Example 601**

**2-METHYL-*N*-[3-(1-{(3*S*)-3-PHENYL-3-[(PROPYLSULFONYL) AMINO] PROPYL}-4-**

**PIPERIDINYL] PHENYL] PROPANAMIDE:** Prepared by Procedure Q1 and Scheme AC using 1-propanesulfonyl chloride and *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 486.2 (*M* + *H*)<sup>+</sup>.



**Example 602**

**N-{3-[1-((3S)-3-{[(3,5-DIMETHYL-4-  
ISOXAZOLYL) SULFONYL] AMINO}-3-PHENYLPROPYL)-4-**

**PIPERIDINYL] PHENYL}-2-METHYLPROPANAMIDE:** Prepared by

5 Procedure Q1 and Scheme AC using 3,5-dimethyl-4-isoxazolesulfonyl chloride and N-(3-{1-[(3S)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide:

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.53 (s, 2H), 7.3-7.1 (m, 5H),  
7.05 (t, 2H, J = 6.5 Hz), 6.81 (d, 1H, J = 7.1 Hz), 4.65  
10 (dd, 1H, J = 6.3, 2.2 Hz), 3.11 (t, 2H, J = 7.2 Hz), 2.4  
(m, 4H), 2.2 (s, 3H), 2.05 (m, 2H), 2.01 (s, 3H), 2.0-  
1.8 (m, 7H), 1.21 (d, 6H, J = 7.1 Hz); ESMS m/e: 539.5  
(M + H)<sup>+</sup>.

15 **Example 603**

**METHYL 3-{[(3-{4-[3-(ISOBUTYRYLAMINO) PHENYL]-1-  
PIPERIDINYL}PROPYL) AMINO] SULFONYL}-2-**

**THIOPHENECARBOXYLATE:** Prepared Procedure Q1 and Scheme  
AC using methyl 3-(chlorosulfonyl)-2-  
20 thiophenecarboxylate and N-{3-[1-(3-aminopropyl)-4-  
piperidinyl]phenyl}-2-methylpropanamide: Anal. Calcd for  
C<sub>24</sub>H<sub>33</sub>N<sub>3</sub>O<sub>5</sub>S.HCl: C, 6.00; H, 5.30; N, 7.72. Found: C,  
52.9; H, 6.04; N, 7.59; ESMS m/e: 508.2 (M + H)<sup>+</sup>.

25 **Example 604**

**2-METHYL-N-{3-[1-((3S)-3-{[(4-  
PHENOXYANILINO) CARBONYL] AMINO}-3-PHENYLPROPYL)-4-**

**PIPERIDINYL] PHENYL}PROPANAMIDE:** Prepared by Procedure P  
and Scheme AB using 1-isocyanato-4-phenoxybenzene and N-  
30 (3-{1-[(3S)-3-amino-3-phenylpropyl]-4-  
piperidinyl}phenyl)-2-methylpropanamide: ESMS m/e: 591.3  
(M + H)<sup>+</sup>.

**PIPERIDINYL] PHENYL}-2-****METHYLPROPANAMIDE:**

Prepared by Procedure Q1 and Scheme AC using 3,5-dimethyl-4-isoxazolesulfonyl chloride and N-(3-{1-[(3S)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-

5 methylpropanamide:  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.53 (s, 2H), 7.3-7.1 (m, 5H), 7.05 (t, 2H,  $J = 6.5$  Hz), 6.81 (d, 1H,  $J = 7.1$  Hz), 4.65 (dd, 1H,  $J = 6.3, 2.2$  Hz), 3.11 (t, 2H,  $J = 7.2$  Hz), 2.4 (m, 4H), 2.2 (s, 3H), 2.05 (m, 2H), 2.01 (s, 3H), 2.0-1.8 (m, 7H), 1.21 (d, 6H,  $J = 7.1$  Hz); ESMS  $m/e$ : 539.5 ( $M + H$ ) $^+$ .

10

**Example 603**

**METHYL 3-{[(3-{4-[3-(ISOBUTYRYLAMINO) PHENYL]-1-PIPERIDINYL}PROPYL) AMINO] SULFONYL}-2-**

15 **THIOPHENECARBOXYLATE:** Prepared Procedure Q1 and Scheme AC using methyl 3-(chlorosulfonyl)-2-thiophenecarboxylate and N-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide: Anal. Calcd for  $\text{C}_{24}\text{H}_{33}\text{N}_3\text{O}_5\text{S} \cdot \text{HCl}$ : C, 6.00; H, 5.30; N, 7.72. Found: C, 20 52.9; H, 6.04; N, 7.59; ESMS  $m/e$ : 508.2 ( $M + H$ ) $^+$ .

**Example 604**

**2-METHYL-N-{3-[1-((3S)-3-{[(4-PHENOXYANILINO) CARBONYL] AMINO}-3-PHENYLPROPYL)-4-**

25 **PIPERIDINYL] PHENYL}PROPANAMIDE:** Prepared by Procedure P and Scheme AB using 1-isocyanato-4-phenoxybenzene and N-(3-{1-[(3S)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS  $m/e$ : 591.3 ( $M + H$ ) $^+$ .

30

**Example 605**

**N-[3-(1-{(3S)-3-[(ANILINOCARBONYL) AMINO]-3-PHENYLPROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure P and Scheme AB using isocyanatobenzene and *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 499.2 (*M* + *H*)<sup>+</sup>.

5

**Example 606**

*N*-(3-[1-((3*S*)-3-{[(*tert*-butylamino) carbonyl] amino}-3-phenylpropyl)-4-piperidinyl]phenyl)-2-methylpropanamide:

Prepared by Procedure P and Scheme AB using 2-isothiocyanato-2-methylpropane and *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 495.1 (*M* + *H*)<sup>+</sup>.

10

**Example 607**

*N*-(3-[1-((3*S*)-3-{[(2-fluoroanilino) carbonyl] amino}-3-phenylpropyl)-4-piperidinyl]phenyl)-2-methylpropanamide:

Prepared by Procedure P and Scheme AB using 1-fluoro-2-isocyanatobenzene and *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 517.0 (*M* + *H*)<sup>+</sup>.

20

**Example 608**

2-METHYL-*N*-(3-(1-{(3*S*)-3-PHENYL-3-[(2-TOLUIDINOCARBOTHIOYL) AMINO] PROPYL}-4-

PIPERIDINYL) PHENYL] PROPANAMIDE: Prepared by Procedure P and Scheme AB using 1-isothiocyanato-2-methylbenzene and *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 529.1 (*M* + *H*)<sup>+</sup>.

30

**Example 609**

*N*-(3-[1-((3*S*)-3-{[(benzylamino) carbonyl] amino}-3-phenylpropyl)-4-piperidinyl]phenyl)-2-methylpropanamide:

phenylpropyl]-4- piperidinyl}phenyl)-2-methylpropanamide:  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.44 (s, 1H), 7.67 (d, 1H,  $J = 7.9$  Hz), 7.31-7.13 (m, 13H), 6.38 (s, 1H), 6.80 (d, 1H,  $J = 7.9$  Hz), 5.54 (m, 1H), 4.81 (m, 1H), 4.41 (dd, 1H,  $J = 14.8, 6.2$  Hz), 4.29 (dd, 1H,  $J = 14.9, 5.4$  Hz), 2.99 (d, 1H,  $J = 11.2$  Hz), 2.87 (d, 1H,  $J = 11.2$  Hz), 2.67 (q, 1H,  $J = 6.2$  Hz), 2.3 (m, 3H), 2.0-1.5 (m, 7H), 1.23 (d, 6H,  $J = 6.7$  Hz); ESMS  $m/e$ : 513.2 ( $M + H$ ) $^+$ .

**Example 610**

2-METHYL-N-{3-[1-((3S)-3-{[(2-NITROANILINO) CARBONYL] AMINO}-3-PHENYLPROPYL)-4-

PIPERIDINYL] PHENYL} PROPANAMIDE: Prepared by Procedure P and Scheme AB using 1-isocyanato-2-nitrobenzene and N-(3-{1-[(3S)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS  $m/e$ : 543.6 ( $M + H$ ) $^+$ .

**Example 611**

N-{3-[1-((3S)-3-{[(3,4-DICHLOROANILINO) CARBONYL] AMINO}-3-PHENYLPROPYL)-4-PIPERIDINYL] PHENYL}-2-

METHYLPROPANAMIDE: Prepared by Procedure P and Scheme AB using 1,2-dichloro-4-isocyanatobenzene and N-(3-{1-[(3S)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS  $m/e$ : 567.1 ( $M + H$ ) $^+$ .

**Example 612**

2-METHYL-N-(3-{1-[(3S)-3-{[(2-

(METHYLSULFANYL) ANILINO] CARBONYL} AMINO)-3-PHENYLPROPYL]-4-PIPERIDINYL} PHENYL) PROPANAMIDE: Prepared by Procedure P and Scheme AB using 1-isocyanato-2-(methylsulfanyl)benzene and N-(3-{1-[(3S)-3-amino-3-

phenylpropyl]-4-

piperidinyl}phenyl)-2-

methylpropanamide: ESMS  $m/e$ : 545.0 ( $M + H$ )<sup>+</sup>.

### Example 613

5 ***N*-{3-[1-(3-{[(4-FLUOROANILINO) CARBONYL] AMINO} PROPYL) -4-PIPERIDINYL] PHENYL}-2-METHYLPROPANAMIDE:** Prepared by Procedure P and Scheme AB using 1-fluoro-4-isocyanatobenzene and *N*-{3-[1-(3-aminopropyl)-4-piperidinyl}phenyl}-2-methylpropanamide: <sup>1</sup>H NMR (400  
10 MHz, CDCl<sub>3</sub>) δ 7.45 (q, 2H,  $J = 4.7$  Hz), 7.23 (m, 4H), 7.05 (t, 4H,  $J = 7.8$  Hz), 6.75 (m, 1H), 4.05 (m, 1H), 3.19 (s, 1H), 2.71 (m, 1H), 2.53 (m, 1H), 2.25 (m, 3H), 1.8 (m, 9H), 1.25 (d, 6H,  $J = 6.4$  Hz); ESMS  $m/e$ : 441.1 ( $M + H$ )<sup>+</sup>.

15

### Example 614

***N*-{3-[1-(3-{[(3,4-DICHLOROANILINO) CARBONYL] AMINO} PROPYL) -4-PIPERIDINYL] PHENYL}-2-METHYLPROPANAMIDE:** Prepared by  
20 Procedure P and Scheme AB using 1,2-dichloro-4-isocyanatobenzene and *N*-{3-[1-(3-aminopropyl)-4-piperidinyl}phenyl}-2-methylpropanamide: ESMS  $m/e$ : 493.2 ( $M + H$ )<sup>+</sup>.

25

### Example 615

**2-METHYL-*N*-[3-(1-{3-[(2-TOLUIDINOCARBOTHIOYL) AMINO] PROPYL}-4-PIPERIDINYL) PHENYL] PROPANAMIDE:** Prepared by Procedure P  
and Scheme AB using 1-isothiocyanato-2-methylbenzene and  
30 *N*-{3-[1-(3-aminopropyl)-4-piperidinyl}phenyl}-2-methylpropanamide: ESMS  $m/e$ : 453.2 ( $M + H$ )<sup>+</sup>.

**Example 616**

**N-{3-[1-(3-{[(BENZYLAMINO) CARBONYL] AMINO} PROPYL)-4-PIPERIDINYL] PHENYL}-2-METHYLPROPANAMIDE:** Prepared by Procedure P and Scheme AB using (isocyanatomethyl)benzene and N-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS m/e: 437.2 (M + H)<sup>+</sup>.

**Example 617**

**N-{3-[1-(3-{[(4-ETHOXYANILINO) CARBONYL] AMINO} PROPYL)-4-PIPERIDINYL] PHENYL}-2-METHYLPROPANAMIDE:** Prepared by Procedure P and Scheme AB using 1-ethoxy-4-isocyanatobenzene and N-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS m/e: 467.2 (M + H)<sup>+</sup>.

**Example 618**

**N-[3-(1-{3-[(ANILINOCARBONYL) AMINO] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure P and Scheme AB using isocyanatobenzene and N-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS m/e: 422.9 (M + H)<sup>+</sup>.

**Example 619**

**2-METHYL-N-(3-{1-[3-({[2-(METHYLSULFANYL) ANILINO] CARBONYL} AMINO) PROPYL]-4-PIPERIDINYL} PHENYL) PROPANAMIDE:** Prepared by Procedure P and Scheme AB using 1-isocyanato-2-(methylsulfanyl)benzene and N-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS m/e: 469.1 (M + H)<sup>+</sup>.

**Example 620**

**N-{3-[1-(3-{[(*TERT*-BUTYLAMINO) CARBOTHIOYL] AMINO} PROPYL)-4-PIPERIDINYL] PHENYL}-2-METHYLPROPANAMIDE:** Prepared by Procedure P and Scheme AB using 2-isothiocyanato-2-methylpropane and N-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 419.0 (M + H)<sup>+</sup>.

**Example 621**

**2-METHYL-N-{3-[1-(3-{[(4-PHENOXYANILINO) CARBONYL] AMINO} PROPYL)-4-PIPERIDINYL] PHENYL} PROPANAMIDE:** Prepared by Procedure P and Scheme AB using 1-isocyanato-4-phenoxybenzene and N-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 515.5 (M + H)<sup>+</sup>.

**Example 622**

**N-(3-{4-[3-(ACETYLAMINO) PHENYL]-1-PIPERIDINYL} PROPYL)-4-(2,4-DIFLUOROPHENYL)-2-METHYL-6-OXO-1,4,5,6-TETRAHYDRO-3-PYRIDINECARBOXAMIDE:** Prepared by Procedure AC and Scheme AM using N-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}acetamide and 4-(2,4-difluorophenyl)-2-methyl-6-oxo-1,4,5,6-tetrahydro-3-pyridinecarboxylic acid: ESMS *m/e*: 525.2 (M + H)<sup>+</sup>.

**Example 623**

**N-(3-{4-[3-(ACETYLAMINO) PHENYL]-1-PIPERIDINYL} PROPYL)-4-(3,4-DIFLUOROPHENYL)-2-METHYL-6-OXO-1,4,5,6-TETRAHYDRO-3-PYRIDINECARBOXAMIDE:** Prepared by Procedure AC and Scheme AM using N-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}acetamide and 4-(3,4-difluorophenyl)-2-methyl-6-oxo-1,4,5,6-tetrahydro-3-pyridinecarboxylic acid: ESMS *m/e*: 525.2 (M + H)<sup>+</sup>.

**Example 624**

**N-(6-{4-[3-(ISOBUTYRYLAMINO) PHENYL]-1-PIPERIDINYL}HEXYL)-1-(4-NITROPHENYL)-5-**

5 **(TRIFLUOROMETHYL)-1H-PYRAZOLE-4-CARBOXAMIDE:** Prepared by Procedure Q1 (THF) and Scheme AT using N-{3-[1-(6-aminohexyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 1-(4-nitrophenyl)-5-(trifluoromethyl)-1H-pyrazole-4-carbonyl chloride: ESMS m/e: 629.2 (M + H)<sup>+</sup>.

10

**Example 625**

**N-[3-(1-{6-[(DIPHENYLACETYL) AMINO] HEXYL}-4-**

15 **PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure Q1 (THF) and Scheme AT using N-{3-[1-(6-aminohexyl)-4-piperidinyl]phenyl}-2-methylpropanamide and diphenylacetyl chloride: ESMS m/e: 540.3 (M + H)<sup>+</sup>.

**Example 626**

**5-(3,5-DICHLOROPHENOXY)-N-(6-{4-[3-**

20 **(ISOBUTYRYLAMINO) PHENYL]-1-PIPERIDINYL}HEXYL)-2-FURAMIDE:**

Prepared by Procedure Q1 (THF) and Scheme AT using N-{3-[1-(6-aminohexyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 5-(3,5-dichlorophenoxy)-2-furoyl chloride: ESMS m/e: 600.2 (M + H)<sup>+</sup>.

25

**Example 627**

**N-(6-{4-[3-(ISOBUTYRYLAMINO) PHENYL]-1-**

30 **PIPERIDINYL}HEXYL)-2-PHENOXYNICOTINAMIDE:** Prepared by Procedure Q1 (THF) and Scheme AT using N-{3-[1-(6-aminohexyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 2-phenoxy nicotinoyl chloride: ESMS m/e: 543.3 (M + H)<sup>+</sup>.



**Example 628**

**N-(6-{4-[3-(ISOBUTYRYLAMINO) PHENYL]-1-**

**PIPERIDINYL}HEXYL)-2-NAPHTHAMIDE:** Prepared by Procedure  
 5 Q1 (THF) and Scheme AT using N-{3-[1-(6-aminohexyl)-4-  
 piperidinyl]phenyl}-2-methylpropanamide and 2-naphthoyl  
 chloride: ESMS  $m/e$ : 500.3 (M + H)<sup>+</sup>.

**Example 629**

10 **1-BENZYL-3-TERT-BUTYL-N-(6-{4-[3-**  
**(ISOBUTYRYLAMINO) PHENYL]-1-PIPERIDINYL}HEXYL)-1H-**  
**PYRAZOLE-5-CARBOXAMIDE:** Prepared by Procedure Q1 (THF)  
 and Scheme AT using N-{3-[1-(6-aminohexyl)-4-  
 piperidinyl]phenyl}-2-methylpropanamide and 1-benzyl-3-  
 15 tert-butyl-1H-pyrazole-5-carbonyl chloride: ESMS  $m/e$ :  
 586.3 (M + H)<sup>+</sup>.

**Example 630**

**3-CHLORO-N-(6-{4-[3-(ISOBUTYRYLAMINO) PHENYL]-1-**  
 20 **PIPERIDINYL}HEXYL)-4-(ISOPROPYLSULFONYL)-2-**  
**THIOPHENECARBOXAMIDE:** Prepared by Procedure Q1 (THF) and  
 Scheme AT using N-{3-[1-(6-aminohexyl)-4-  
 piperidinyl]phenyl}-2-methylpropanamide and 3-chloro-4-  
 (isopropylsulfonyl)-2-thiophenecarbonyl chloride: ESMS  
 25  $m/e$ : 596.2 (M + H)<sup>+</sup>.

**Example 631**

**N-[3-(1-{6-[(ANILINOCARBONYL) AMINO] HEXYL}-4-**  
**PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:** Prepared by  
 30 Procedure Q1 (THF) and Scheme AT using N-{3-[1-(6-  
 aminohexyl)-4-piperidinyl]phenyl}-2-methylpropanamide  
 and phenyl isocyanate : ESMS  $m/e$ : 465.2 (M + H)<sup>+</sup>.

**Example 632**

**N-{3-[1-(6-{[(2,4-DICHLOROANILINO) CARBONYL] AMINO}HEXYL)-4-PIPERIDINYL] PHENYL}-2-METHYLPROPANAMIDE:** Prepared by Procedure Q1 (THF) and Scheme AT using N-{3-[1-(6-aminohexyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 2,4-dichlorophenyl isocyanate: ESMS m/e: 533.2 (M + H)<sup>+</sup>.

**Example 633**

**N-(6-{4-[3-(ISOBUTYRYLAMINO) PHENYL]-1-PIPERIDINYL}HEXYL)-1-PHENYL-5-PROPYL-1H-PYRAZOLE-4-CARBOXAMIDE:** Prepared by Procedure Q1 (THF) and Scheme AT using N-{3-[1-(6-aminohexyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 1-phenyl-5-propyl-1H-pyrazole-4-carbonyl chloride: ESMS m/e: 558.3 (M + H)<sup>+</sup>.

**Example 634**

**2-METHYL-N-{3-[1-(6-{[(1-NAPHTHYLAMINO) CARBONYL] AMINO}HEXYL)-4-PIPERIDINYL] PHENYL}PROPANAMIDE:** Prepared by Procedure Q1 (THF) and Scheme AT using N-{3-[1-(6-aminohexyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 1-naphthyl isocyanate: ESMS m/e: 515.3 (M + H)<sup>+</sup>.

**Example 635**

**N-{3-[1-(6-{[(1,1'-BIPHENYL)-4-YLAMINO) CARBONYL] AMINO}HEXYL)-4-PIPERIDINYL] PHENYL}-2-METHYLPROPANAMIDE:** Prepared by Procedure Q1 (THF) and Scheme AT using N-{3-[1-(6-aminohexyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 4-biphenyl isocyanate: ESMS m/e: 541.3 (M + H)<sup>+</sup>.

**Example 636**

2-METHYL-N-{3-[1-(6-{[(2-NAPHTHYLAMINO) CARBONYL] AMINO}HEXYL)-4-

PIPERIDINYL] PHENYL} PROPANAMIDE: Prepared by Procedure Q1 (THF) and Scheme AT using N-{3-[1-(6-aminohexyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 2-naphthyl isocyanate: ESMS  $m/e$ : 515.3 (M + H)<sup>+</sup>.

#### Example 637

N-{3-[1-(3-{[(3,4-DIMETHOXYPHENYL) SULFONYL] AMINO}PROPYL)-4-PIPERIDINYL] PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure Q1 (THF) and Scheme AT using N-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 3,4-dimethoxybenzenesulfonyl chloride: ESMS  $m/e$ : 504.2 (M + H)<sup>+</sup>.

#### Example 638

N-(3-{4-[3-(ISOBUTYRYLAMINO) PHENYL]-1-PIPERIDINYL}PROPYL)-5-METHYL-3-PHENYL-4-ISOXAZOLECARBOXAMIDE: Prepared by Procedure Q1 (THF) and Scheme AT using N-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 5-methyl-3-phenyl-4-isoxazolecarbonyl chloride: ESMS  $m/e$ : 489.3 (M + H)<sup>+</sup>.

#### Example 639

N-{3-[1-(3-{[(4-FLUOROPHENYL) ACETYL] AMINO}PROPYL)-4-PIPERIDINYL] PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure Q1 (THF) and Scheme AT using N-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide and (4-fluorophenyl)acetyl chloride: ESMS  $m/e$ : 440.3 (M + H)<sup>+</sup>.

**Example 640**

**N-{3-[1-(3-{[(4-CHLORO-3-NITROPHENYL) SULFONYL] AMINO} PROPYL) -4-PIPERIDINYL] PHENYL}-2-METHYLPROPANAMIDE:**

Prepared by Procedure Q1 (THF) and Scheme AT using N-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 4-chloro-3-nitrobenzenesulfonyl chloride: ESMS  $m/e$ : 523.1 (M + H)<sup>+</sup>.

10 **Example 641**

**2-(4-CHLOROPHENOXY)-N-(3-{4-[3-(ISOBUTYRYLAMINO) PHENYL]-1-PIPERIDINYL} PROPYL) NICOTINAMIDE:** Prepared by Procedure Q1 (THF) and Scheme AT using N-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 2-(4-chlorophenoxy)nicotinoyl chloride: ESMS  $m/e$ : 535.2 (M + H)<sup>+</sup>.

**Example 642**

**5-(3,5-DICHLOROPHENOXY)-N-(3-{4-[3-(ISOBUTYRYLAMINO) PHENYL]-1-PIPERIDINYL} PROPYL)-2-FURAMIDE:**

Prepared by Procedure Q1 (THF) and Scheme AT using N-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 5-(3,5-dichlorophenoxy)-2-furoyl chloride: ESMS  $m/e$ : 558.2 (M + H)<sup>+</sup>.

**Example 643**

**N-{3-[1-(3-{[(2-FLUOROPHENYL) SULFONYL] AMINO} PROPYL) -4-PIPERIDINYL] PHENYL}-2-METHYLPROPANAMIDE:**

Prepared by Procedure Q1 (THF) and Scheme AT using N-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 2-fluorobenzenesulfonyl chloride: ESMS  $m/e$ : 462.2 (M + H)<sup>+</sup>.

**Example 644**

**N-{3-[1-(3-{[(3,5-DIMETHYL-4-**

**ISOXAZOLYL) SULFONYL] AMINO} PROPYL) -4-PIPERIDINYL] PHENYL}-**

5 **2-METHYLPROPANAMIDE:** Prepared by Procedure Q1 (THF) and Scheme AT using N-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 3,5-dimethyl-4-isoxazolesulfonyl chloride: ESMS *m/e*: 463.2 (M + H)<sup>+</sup>.

10

**Example 644**

**N-{3-[1-(3-{[(4-TERT-BUTYLPHENYL) SULFONYL] AMINO} PROPYL) -**

**4-PIPERIDINYL] PHENYL}-2-METHYLPROPANAMIDE:** Prepared by

15 Procedure Q1 (THF) and Scheme AT using N-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 4-tert-butylbenzenesulfonyl chloride: ESMS *m/e*: 500.3 (M + H)<sup>+</sup>.

**Example 646**

20 **N-{3-[1-(6-AMINOHEXYL) -4-PIPERIDINYL] PHENYL}-2-**

**METHYLPROPANAMIDE:** Prepared by Procedure AE and Scheme Y using N-(3-{1-[6-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)hexyl]-4-piperidinyl}phenyl)-2-methylpropanamide and hydrazine hydrate: ESMS *m/e*: 346.2 (M + H)<sup>+</sup>.

25

**Example 647**

**N-{3-[1-(2-{[([1,1'-BIPHENYL] -4-**

**YLAMINO) CARBONYL] AMINO} ETHYL) -4-PIPERIDINYL] PHENYL}-2-**

30 **METHYLPROPANAMIDE:** Prepared by Procedure Q1 (THF) and Scheme AT using N-{3-[1-(2-aminoethyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 4-biphenyl isocyanate: ESMS *m/e*: 485.2 (M + H)<sup>+</sup>.

**Example 648**

5- (3,5-DICHLOROPHENOXY) -N-(2-{4-[3-(ISOBUTYRYLAMINO) PHENYL] -1-PIPERIDINYL}ETHYL) -3-FURAMIDE:

5 Prepared by Procedure Q1 (THF) and Scheme AT using N-{3-[1-(2-aminoethyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 5-(3,5-dichlorophenoxy)-3-furoyl chloride: ESMS m/e: 544.1 (M + H)<sup>+</sup>.

10 **Example 649**

N-[3-(1-{2-[(DIPHENYLACETYL) AMINO] ETHYL}-4-PIPERIDINYL) PHENYL] -2-METHYLPROPANAMIDE:

Prepared by Procedure Q1 (THF) and Scheme AT using N-{3-[1-(2-aminoethyl)-4-piperidinyl]phenyl}-2-methylpropanamide and diphenylacetyl chloride: ESMS m/e: 484.2 (M + H)<sup>+</sup>.

**Example 650**

N-(2-{4-[3-(ISOBUTYRYLAMINO) PHENYL] -1-PIPERIDINYL}ETHYL) -2-NAPHTHAMIDE:

20 Prepared by Procedure Q1 (THF) and Scheme AT using N-{3-[1-(2-aminoethyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 2-naphthoyl chloride: ESMS m/e: 444.2 (M + H)<sup>+</sup>.

**Example 651**

25 3-(2,6-DICHLOROPHENYL) -N-(4-{4-[3-(ISOBUTYRYLAMINO) PHENYL] -1-PIPERIDINYL}BUTYL) -5-METHYL-4-ISOXAZOLECARBOXAMIDE:

Prepared by Procedure Q1 (THF) and Scheme AT using N-{3-[1-(4-aminobutyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 3-(2,6-dichlorophenyl)-5-methyl-4-isoxazolecarbonyl chloride: ESMS m/e: 571.2 (M + H)<sup>+</sup>.

**Example 652**

3-(2,6-DICHLOROPHENYL)-N-(5-{4-[3-(ISOBUTYRYLAMINO) PHENYL]-1-PIPERIDINYL}PENTYL)-5-METHYL-4-ISOXAZOLECARBOXAMIDE:

Prepared by Procedure Q1 (THF) and Scheme AT using N-{3-[1-(5-aminopentyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 3-(2,6-dichlorophenyl)-5-methyl-4-isoxazolecarbonyl chloride. ESMS  $m/e$ : 585.2 (M + H)<sup>+</sup>.

#### Example 653

10 N-[3-(1-{4-[(DIPHENYLACETYL) AMINO] BUTYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure Q2 (THF/DCM, 1:3) and Scheme AT using N-{3-[1-(4-aminobutyl)-4-piperidinyl]phenyl}-2-methylpropanamide and diphenylacetyl chloride: ESMS  $m/e$ : 512.0 (M + H)<sup>+</sup>.

#### Example 654

20 N-[3-(1-{5-[(DIPHENYLACETYL) AMINO] PENTYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure Q2 (THF/DCM, 1:3) and Scheme AT using N-{3-[1-(5-aminopentyl)-4-piperidinyl]phenyl}-2-methylpropanamide and diphenylacetyl chloride: ESMS  $m/e$ : 526.0 (M + H)<sup>+</sup>.

#### 25 Example 655

3,5-DICHLORO-N-(4-{4-[3-(ISOBUTYRYLAMINO) PHENYL]-1-PIPERIDINYL}BUTYL) BENZAMIDE: Prepared by Procedure Q2 (THF/DCM, 1:3) and Scheme AT using N-{3-[1-(4-aminobutyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 3,5-dichlorobenzoyl chloride: ESMS  $m/e$ : 490.0 (M + H)<sup>+</sup>.

#### Example 656

5-(3,5-DICHLOROPHENOXY)-N-(4-{4-[3-(ISOBUTYRYLAMINO) PHENYL]-1-PIPERIDINYL} BUTYL)-2-

**FURAMIDE:**

Prepared by Procedure Q2 (THF/DCM, 1:3) and Scheme AT using N-{3-[1-(4-aminobutyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 5-(3,5-dichlorophenoxy)-2-furoyl chloride: ESMS m/e: 572.0 (M + H)<sup>+</sup>.

**Example 657**

3-CHLORO-N-(4-{4-[3-(ISOBUTYRYLAMINO) PHENYL]-1-PIPERIDINYL} BUTYL) BENZAMIDE: Prepared by Procedure Q2 (THF/DCM, 1:3) and Scheme AT using N-{3-[1-(4-aminobutyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 3-chlorobenzoyl chloride: ESMS m/e: 456.0 (M + H)<sup>+</sup>.

**Example 658**

3,4-DIFLUORO-N-(4-{4-[3-(ISOBUTYRYLAMINO) PHENYL]-1-PIPERIDINYL} BUTYL) BENZAMIDE: Prepared by Procedure Q2 (THF/DCM, 1:3) and Scheme AT using N-{3-[1-(4-aminobutyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 3,4-difluorobenzoyl chloride: ESMS m/e: 458.0 (M + H)<sup>+</sup>.

**Example 659**

N-{3-[1-(4-{[(3,5-DICHLOROANILINO) CARBONYL] AMINO} BUTYL)-4-PIPERIDINYL] PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure Q2 (THF/DCM, 1:3) and Scheme AT using N-(3-{1-[4-(formylamino) butyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 3,5-dichlorophenyl isocyanate: ESMS m/e: 505.0 (M + H)<sup>+</sup>.

**Example 660**



**N-{3-[1-(4-{([1,1'-BIPHENYL]-4-YLAMINO) CARBONYL} AMINO) BUTYL)-4-PIPERIDINYL} PHENYL}-2-METHYLPROPANAMIDE:** Prepared by Procedure Q2 (THF/DCM, 1:3) and Scheme AT using N-{3-[1-(4-aminobutyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 4-biphenyl isocyanate: ESMS  $m/e$ : 513.0 (M + H)<sup>+</sup>.

**Example 661**

**2-METHYL-N-(3-{1-[5-(4-NITROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL} PHENYL) PROPANAMIDE:**

Prepared by Procedure K and Scheme B1 (K<sub>2</sub>CO<sub>3</sub>) using 5-chloro-1-(4-nitrophenyl)-1-pentanone and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 452.2 (M + H)<sup>+</sup>.

**Example 662**

**N-(3-{1-[5-(4-FLUOROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL} PHENYL)-2-METHYLPROPANAMIDE:**

Prepared by Procedure K and Scheme B1 (K<sub>2</sub>CO<sub>3</sub>) using 5-chloro-1-(4-fluorophenyl)-1-pentanone and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 425.2 (M + H)<sup>+</sup>.

**Example 663**

**2-METHYL-N-[3-(1-{5-OXO-5-[2-(TRIFLUOROMETHYL) PHENYL] PENTYL}-4-PIPERIDINYL) PHENYL] PROPANAMIDE:**

Prepared by Procedure K and Scheme B1 (K<sub>2</sub>CO<sub>3</sub>) using 5-chloro-1-[2-(trifluoromethyl)phenyl]-1-pentanone and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 475.2 (M + H)<sup>+</sup>.

**Example 664**

**N-(3-{1-[5-(3-BROMOPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL} PHENYL)-2-METHYLPROPANAMIDE:**

Prepared by

Procedure K and Scheme B1 ( $K_2CO_3$ ) using 1-(3-bromophenyl)-5-chloro-1-pentanone and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 485.1 ( $M + H$ )<sup>+</sup>.

5 **Example 665**

2-METHYL-N-(3-{1-[5-(3-NITROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure K and Scheme B1 ( $K_2CO_3$ ) using 5-chloro-1-(3-nitrophenyl)-1-pentanone and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 452.2 ( $M + H$ )<sup>+</sup>.

**Example 666**

N-(3-{1-[5-(3-CHLOROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure K and Scheme B1 ( $K_2CO_3$ ) using 1-(3-chlorophenyl)-5-chloro-1-pentanone and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 441.1 ( $M + H$ )<sup>+</sup>.

**Example 667**

20 N-(3-{1-[5-(4-BROMOPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure K and Scheme B1 ( $K_2CO_3$ ) using 1-(4-bromophenyl)-5-chloro-1-pentanone and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 485.1 ( $M + H$ )<sup>+</sup>.

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**Example 668**

30 N-(3-{1-[5-(2-IODOPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure K and Scheme B1 ( $K_2CO_3$ ) using 1-(2-iodophenyl)-5-chloro-1-pentanone and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 533.0 ( $M + H$ )<sup>+</sup>.

**Example 669**

**N-(3-{1-[5-(3-FLUOROPHENYL)-5-  
OXOPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:**

Prepared by Procedure K and Scheme B1 ( $K_2CO_3$ ) using 1-(3-fluorophenyl)-5-chloro-1-pentanone and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 425.2 ( $M + H$ )<sup>+</sup>.

**Example 670**

**2-METHYL-N-[3-(1-{5-  
10 (TRIFLUOROMETHYL)PHENYL]PENTYL}-4-  
PIPERIDINYL)PHENYL]PROPANAMIDE:** Prepared by Procedure K and Scheme B1 ( $K_2CO_3$ ) using 1-[3-(trifluoromethyl)phenyl]-5-chloro-1-pentanone and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ :  
15 475.2 ( $M + H$ )<sup>+</sup>.

**Example 671**

**N-(3-{1-[5-(2-FLUOROPHENYL)-5-  
OXOPENTYL]-4-  
PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by  
20 Procedure K and Scheme B1 ( $K_2CO_3$ ) using 1-(2-fluorophenyl)-5-chloro-1-pentanone and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 425.2 ( $M + H$ )<sup>+</sup>.

**Example 672**

**N-(3-{1-[5-(3-  
25 IODOPHENYL)-5-  
OXOPENTYL]-4-  
PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by  
Procedure K and Scheme B1 ( $K_2CO_3$ ) using 1-(3-iodophenyl)-5-chloro-1-pentanone and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 533.0 ( $M + H$ )<sup>+</sup>.

30

**Example 673**

**N-(3-{1-[5-(2-  
CHLOROPHENYL)-5-  
OXOPENTYL]-4-  
PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by

Procedure K and Scheme B1 ( $K_2CO_3$ ) using 1-(2-chlorophenyl)-5-chloro-1-pentanone and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 441.1 ( $M + H$ )<sup>+</sup>.

5 **Example 674**

2-METHYL-N-[3-(1-{5-OXO-5-[4-(TRIFLUOROMETHYL) PHENYL] PENTYL}-4-

10 PIPERIDINYL) PHENYL] PROPANAMIDE: Prepared by Procedure K and Scheme B1 ( $K_2CO_3$ ) using 1-[4-(trifluoromethyl)phenyl]-5-chloro-1-pentanone and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 475.2 ( $M + H$ )<sup>+</sup>.

**Example 675**

15 N-(3-{1-[5-(4-CHLOROPHENYL)-5-OXOPENTYL]-4-

PIPERIDINYL} PHENYL) -2-METHYLPROPANAMIDE: Prepared by Procedure K and Scheme B1 ( $K_2CO_3$ ) using 1-(4-chlorophenyl)-5-chloro-1-pentanone and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 441.1 ( $M + H$ )<sup>+</sup>.

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**Example 676**

N-(3-{1-[5-(4-IODOPHENYL)-5-OXOPENTYL]-4-

25 PIPERIDINYL} PHENYL) -2-METHYLPROPANAMIDE: Prepared by Procedure K and Scheme B1 ( $K_2CO_3$ ) using 1-(4-iodophenyl)-5-chloro-1-pentanone and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 533 ( $M + H$ )<sup>+</sup>.

**Example 677**

30 N-(3-{1-[5-(2-BROMOPHENYL)-5-OXOPENTYL]-4-

PIPERIDINYL} PHENYL) -2-METHYLPROPANAMIDE: Prepared by Procedure K and Scheme B1 ( $K_2CO_3$ ) using 1-(2-bromophenyl)-5-chloro-1-pentanone and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 485.1 ( $M + H$ )<sup>+</sup>.

**Example 678**

2-(4-CHLOROPHENOXY)-N-(4-{4-[3-(ISOBUTYRYLAMINO) PHENYL]-  
 1-PIPERIDINYL}BUTYL)NICOTINAMIDE: Prepared by Procedure  
 5 Q2 (THF/DCM, 1:3) and Scheme AT using N-{3-[1-(4-  
 aminobutyl)-4-piperidinyl]phenyl}-2-methylpropanamide  
 and 2-(4-chlorophenoxy)nicotinoyl chloride: ESMS m/e:  
 549.0 (M + H)<sup>+</sup>.

10 **Example 679**

N-(4-{4-[3-(ISOBUTYRYLAMINO) PHENYL]-1-  
 PIPERIDINYL}BUTYL)-3,4-DIMETHOXYBENZAMIDE: Prepared by  
 Procedure Q2 (THF/DCM, 1:3) and Scheme AT using N-{3-  
 [1-(4-aminobutyl)-4-piperidinyl]phenyl}-2-  
 15 methylpropanamide and 3,4-dimethoxybenzoyl chloride:  
 ESMS m/e: 482.0 (M + H)<sup>+</sup>.

**Example 680**

3-(2-CHLOROPHENYL)-N-(4-{4-[3-(ISOBUTYRYLAMINO) PHENYL]-  
 20 1-PIPERIDINYL}BUTYL)-5-METHYL-4-ISOXAZOLECARBOXAMIDE:  
 Prepared by Procedure Q2 (THF/DCM, 1:3) and Scheme AT  
 using N-{3-[1-(4-aminobutyl)-4-piperidinyl]phenyl}-2-  
 methylpropanamide and 3-(2-chlorophenyl)-5-methyl-4-  
 isoxazolecarbonyl chloride: ESMS m/e: 537.0 (M + H)<sup>+</sup>.

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**Example 681**

3-(2-CHLOROPHENYL)-N-(5-{4-[3-(ISOBUTYRYLAMINO) PHENYL]-  
 1-PIPERIDINYL}PENTYL)-5-METHYL-4-ISOXAZOLECARBOXAMIDE:  
 Prepared by Procedure Q2 (THF/DCM, 1:3) and Scheme AT  
 using N-{3-[1-(5-aminopentyl)-4-piperidinyl]phenyl}-2-  
 30 methylpropanamide and 3-(2-chlorophenyl)-5-methyl-4-  
 isoxazolecarbonyl chloride: ESMS m/e: 551.0 (M + H)<sup>+</sup>.

**Example 682**

2-METHYL-N-{3-[1-(3-{1-METHYL-2-[4-(TRIFLUOROMETHYL) PHENYL]-1H-INDOL-3-YL}PROPYL)-4-PIPERIDINYL] PHENYL}PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-N-[3-(1-{5-oxo-5-[4-(trifluoromethyl)phenyl]pentyl}-4-piperidinyl)phenyl]propanamide and 1-methyl-1-phenylhydrazine: ESMS  $m/e$ : 562.2 ( $M + H$ )<sup>+</sup>.

**Example 683**

2-METHYL-N-{3-[1-(3-{1-METHYL-2-[4-(TRIFLUOROMETHYL) PHENYL]-1H-INDOL-3-YL}PROPYL)-4-PIPERIDINYL] PHENYL}PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-N-[3-(1-{5-oxo-5-[4-(trifluoromethyl)phenyl]pentyl}-4-piperidinyl)phenyl]propanamide and 4-(trifluoromethoxy)phenylhydrazine hydrochloride: ESMS  $m/e$ : 632.2 ( $M + H$ )<sup>+</sup>.

**Example 684**

2-METHYL-N-{3-[1-(3-{2-[4-(TRIFLUOROMETHYL) PHENYL]-1H-INDOL-3-YL}PROPYL)-4-PIPERIDINYL] PHENYL}PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-N-[3-(1-{5-oxo-5-[4-(trifluoromethyl)phenyl]pentyl}-4-piperidinyl)phenyl]propanamide and phenylhydrazine: ESMS  $m/e$ : 548.2 ( $M + H$ )<sup>+</sup>.

**Example 685**

2-METHYL-N-{3-[1-(3-{1-PHENYL-2-[4-(TRIFLUOROMETHYL) PHENYL]-1H-INDOL-3-YL}PROPYL)-4-PIPERIDINYL] PHENYL}PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-N-[3-(1-{5-oxo-5-[4-(trifluoromethyl)phenyl]pentyl}-4-

piperidinyl)phenyl]propanamide and 1,1-diphenylhydrazine hydrochloride: ESMS  $m/e$ : 624.2 ( $M + H$ )<sup>+</sup>.

**Example 686**

5 2-METHYL-N-{3-[1-(3-{2-[4-(TRIFLUOROMETHYL) PHENYL]-1H-BENZO[G]INDOL-3-YL}PROPYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-N-[3-(1-{5-oxo-5-[4-(trifluoromethyl)phenyl]pentyl}-4-piperidinyl)phenyl]propanamide and 1-naphthylhydrazine  
10 hydrochloride: ESMS  $m/e$ : 598.2 ( $M + H$ )<sup>+</sup>.

**Example 687**

2-METHYL-N-{3-[1-(3-{7-METHYL-2-[4-(TRIFLUOROMETHYL) PHENYL]-1H-INDOL-3-YL}PROPYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-N-[3-(1-{5-oxo-5-[4-(trifluoromethyl)phenyl]pentyl}-4-piperidinyl)phenyl]propanamide and 1-(2-methylphenyl)hydrazine hydrochloride: ESMS  $m/e$ : 562.2 ( $M + H$ )<sup>+</sup>.  
15  
20

**Example 688**

2-METHYL-N-{3-[1-(3-{5-METHYL-2-[4-(TRIFLUOROMETHYL) PHENYL]-1H-INDOL-3-YL}PROPYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-N-[3-(1-{5-oxo-5-[4-(trifluoromethyl)phenyl]pentyl}-4-piperidinyl)phenyl]propanamide and 4-methylphenylhydrazine hydrochloride: ESMS  $m/e$ : 562.2 ( $M + H$ )<sup>+</sup>.  
25  
30

**Example 689**

N-{3-[1-(3-{5-METHOXY-2-(TRIFLUOROMETHYL)PHENYL}-1H-INDOL-3-YL)PROPYL]-4-PIPERIDINYL}PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-N-[3-(1-{5-oxo-5-[4-(trifluoromethyl)phenyl]pentyl}-4-piperidinyl)phenyl]propanamide and 4-methoxyphenylhydrazine hydrochloride: ESMS  $m/e$ : 578.2 ( $M + H$ )<sup>+</sup>.

10 **Example 690**

N-[3-(1-{3-[2-(3-FLUOROPHENYL)-7-METHYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using N-(3-{1-[5-(3-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-(2-methylphenyl)hydrazine hydrochloride: ESMS  $m/e$ : 512.2 ( $M + H$ )<sup>+</sup>.

**Example 691**

20 N-[3-(1-{3-[2-(4-CHLOROPHENYL)-1-METHYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using N-(3-{1-[5-(4-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-methyl-1-phenylhydrazine: ESMS  $m/e$ : 528.2 ( $M + H$ )<sup>+</sup>.

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**Example 692**

30 N-[3-(1-{3-[2-(4-FLUOROPHENYL)-5-METHOXY-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using N-(3-{1-[5-(4-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-methoxyphenylhydrazine hydrochloride: ESMS  $m/e$ : 528.2 ( $M + H$ )<sup>+</sup>.



**Example 693**

**N-[3-(1-{3-[2-(2-FLUOROPHENYL)-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure E and Scheme M using N-(3-{1-[5-(2-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and phenylhydrazine: ESMS m/e: 498.2 (M + H)<sup>+</sup>.

**Example 694**

**N-[3-(1-{3-[2-(3-FLUOROPHENYL)-5-(TRIFLUOROMETHOXY)-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure E and Scheme M using N-(3-{1-[5-(3-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-(trifluoromethoxy)phenylhydrazine hydrochloride: ESMS m/e: 582.2 (M + H)<sup>+</sup>.

**Example 695**

**N-[3-(1-{3-[2-(2-FLUOROPHENYL)-5-(TRIFLUOROMETHOXY)-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure E and Scheme M using N-(3-{1-[5-(2-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-(trifluoromethoxy)phenylhydrazine hydrochloride: ESMS m/e: 582.2 (M + H)<sup>+</sup>.

**Example 696**

**N-[3-(1-{3-[2-(4-FLUOROPHENYL)-1-PHENYL-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure E and Scheme M using N-(3-{1-[5-(4-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1,1-diphenylhydrazine hydrochloride: ESMS m/e: 548.2 (M + H)<sup>+</sup>.

**Example 697**

***N*-[3-(1-{3-[2-(2-FLUOROPHENYL)-1*H*-BENZO[G]INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-naphthylhydrazine hydrochloride:  
 5 ESMS *m/e*: 547.7 (*M* + *H*)<sup>+</sup>.

**Example 698**

10 ***N*-[3-(1-{3-[2-(2-FLUOROPHENYL)-5-METHYL-1*H*-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-methylphenylhydrazine  
 15 hydrochloride: ESMS *m/e*: 512.2 (*M* + *H*)<sup>+</sup>.

**Example 699**

***N*-[3-(1-{3-[2-(3-FLUOROPHENYL)-1*H*-BENZO[G]INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:**

20 Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-naphthylhydrazine hydrochloride:  
 ESMS *m/e*: 548.2 (*M* + *H*)<sup>+</sup>.

**Example 700**

25 ***N*-[3-(1-{3-[2-(4-FLUOROPHENYL)-1-METHYL-1*H*-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-methyl-1-phenylhydrazine:  
 30 ESMS *m/e*: 512.2 (*M* + *H*)<sup>+</sup>.

**Example 701**

**N-[3-(1-{3-[2-(3-FLUOROPHENYL)-5-METHOXY-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using N-(3-{1-[5-(3-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-methoxyphenylhydrazine hydrochloride: ESMS m/e: 528.2 (M + H)<sup>+</sup>.

**Example 702**

**N-[3-(1-{3-[2-(3-FLUOROPHENYL)-1-PHENYL-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using N-(3-{1-[5-(3-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1,1-diphenylhydrazine hydrochloride: ESMS m/e: 574.2 (M + H)<sup>+</sup>.

**Example 703**

**N-[3-(1-{3-[2-(4-CHLOROPHENYL)-5-(TRIFLUOROMETHOXY)-1H-INDOL-3-YL] PROPYL}-4-**

**PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure E and Scheme M using N-(3-{1-[5-(4-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-(trifluoromethoxy)phenylhydrazine hydrochloride: ESMS m/e: 598.2 (M + H)<sup>+</sup>.

**Example 704**

**N-[3-(1-{3-[2-(3-FLUOROPHENYL)-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:** Prepared by

Procedure E and Scheme M using N-(3-{1-[5-(3-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and phenylhydrazine: ESMS m/e: 498.2 (M + H)<sup>+</sup>.

**Example 705**

**N-[3-(1-{3-[2-(3-FLUOROPHENYL)-1-METHYL-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**

5 Prepared by Procedure E and Scheme M using N-(3-{1-[5-(3-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-methyl-1-phenylhydrazine: ESMS  $m/e$ : 512.2 (M + H)<sup>+</sup>.

10 **Example 706**

**N-[3-(1-{3-[2-(3-FLUOROPHENYL)-5-METHYL-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using N-(3-{1-[5-(3-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-  
15 methylpropanamide and 4-methylphenylhydrazine hydrochloride: ESMS  $m/e$ : 512.2 (M + H)<sup>+</sup>.

**Example 707**

**N-[3-(1-{3-[2-(4-CHLOROPHENYL)-1H-BENZO[G]INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**

20 Prepared by Procedure E and Scheme M using N-(3-{1-[5-(4-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-naphthylhydrazine hydrochloride: ESMS  $m/e$ : 564.2 (M + H)<sup>+</sup>.

25

**Example 708**

**N-[3-(1-{3-[2-(4-CHLOROPHENYL)-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:** Prepared by  
Procedure E and Scheme M using N-(3-{1-[5-(4-  
30 chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-phenylhydrazine hydrochloride: ESMS  $m/e$ : 514.2 (M + H)<sup>+</sup>.

**Example 709**

***N*-[3-(1-{3-[2-(2-FLUOROPHENYL)-1-METHYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-methyl-1-phenylhydrazine: ESMS  $m/e$ : 512.2 ( $M + H$ )<sup>+</sup>.

**Example 710**

***N*-[3-(1-{3-[2-(2-FLUOROPHENYL)-7-METHYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-(2-methylphenyl)hydrazine hydrochloride: ESMS  $m/e$ : 512.2 ( $M + H$ )<sup>+</sup>.

**Example 711**

***N*-[3-(1-{3-[2-(2-FLUOROPHENYL)-1-PHENYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1,1-diphenylhydrazine hydrochloride: ESMS  $m/e$ : 574.2 ( $M + H$ )<sup>+</sup>.

**Example 712**

***N*-[3-(1-{3-[2-(2-FLUOROPHENYL)-5-METHOXY-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-methoxyphenylhydrazine hydrochloride: ESMS  $m/e$ : 528.2 ( $M + H$ )<sup>+</sup>.

**Example 713**

**N- [3- (1- {3- [2- (4- CHLOROPHENYL) -5-METHOXY-  
1H-INDOL-3-YL] PROPYL} -4-PIPERIDINYL) PHENYL] -2-  
METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using N-(3-{1-[5-  
5 (4-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-  
methylpropanamide and 4-methoxyphenylhydrazine  
hydrochloride: ESMS  $m/e$ : 544.2 (M + H)<sup>+</sup>.

**Example 714**

10 **N- [3- (1- {3- [2- (4-FLUOROPHENYL) -1H-BENZO [G] INDOL-3-  
YL] PROPYL} -4-PIPERIDINYL) PHENYL] -2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using N-(3-{1-[5-  
(4-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-  
methylpropanamide and 1-naphthylhydrazine hydrochloride:  
15 ESMS  $m/e$ : 548.2 (M + H)<sup>+</sup>.

**Example 715**

**N- [3- (1- {3- [2- (4-FLUOROPHENYL) -5- (TRIFLUOROMETHOXY) -1H-  
INDOL-3-YL] PROPYL} -4-PIPERIDINYL) PHENYL] -2-  
20 METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using N-(3-{1-[5-  
(4-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-  
methylpropanamide and 4-  
(trifluoromethoxy)phenylhydrazine hydrochloride: ESMS  
25  $m/e$ : 582.9 (M + H)<sup>+</sup>.

**Example 716**

**N- [3- (1- {3- [2- (4-FLUOROPHENYL) -7-METHYL-1H-INDOL-3-  
YL] PROPYL} -4-PIPERIDINYL) PHENYL] -2-METHYLPROPANAMIDE:**

30 Prepared by Procedure E and Scheme M using N-(3-{1-[5-  
(4-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-  
methylpropanamide and 1-(2-methylphenyl)hydrazine  
hydrochloride: ESMS  $m/e$ : 512.2 (M + H)<sup>+</sup>.

**Example 717**

**N-[3-(1-{3-[2-(4-FLUOROPHENYL)-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:** Prepared by  
 5 Procedure E and Scheme M using N-(3-{1-[5-(4-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and phenylhydrazine: ESMS m/e: 498.2 (M + H)<sup>+</sup>.

**Example 718**

10 **N-[3-(1-{3-[2-(4-FLUOROPHENYL)-5-METHYL-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**  
 Prepared by Procedure E and Scheme M using N-(3-{1-[5-(4-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-  
 15 methylpropanamide and 4-methylphenylhydrazine hydrochloride: ESMS m/e: 512.2 (M + H)<sup>+</sup>.

**Example 719**

20 **N-[3-(1-{3-[2-(4-CHLOROPHENYL)-7-METHYL-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**  
 Prepared by Procedure E and Scheme M using N-(3-{1-[5-(4-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-(2-methylphenyl)hydrazine hydrochloride: ESMS m/e: 528.2 (M + H)<sup>+</sup>.

**Example 720**

25 **N-[3-(1-{3-[2-(4-CHLOROPHENYL)-5-METHYL-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**  
 Prepared by Procedure E and Scheme M using N-(3-{1-[5-(4-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-  
 30 methylpropanamide and 4-methylphenylhydrazine hydrochloride: ESMS m/e: 528.2 (M + H)<sup>+</sup>.

**Example 721**

**N-[3-(1-{3-[2-(4-CHLOROPHENYL)-1-PHENYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using N-(3-{1-[5-(4-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1,1-diphenylhydrazine hydrochloride: ESMS  $m/e$ : 590.2 ( $M + H$ )<sup>+</sup>.

**Example 722**

10 **N-[3-(1-{3-[2-(3-CHLOROPHENYL)-7-METHYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using N-(3-{1-[5-(3-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-(2-methylphenyl)hydrazine hydrochloride: ESMS  $m/e$ : 528.1 ( $M + H$ )<sup>+</sup>.

**Example 723**

20 **N-[3-(1-{3-[2-(3-CHLOROPHENYL)-5-(TRIFLUOROMETHOXY)-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using N-(3-{1-[5-(3-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-(trifluoromethoxy)phenylhydrazine hydrochloride: ESMS  $m/e$ : 598.2 ( $M + H$ )<sup>+</sup>.

**Example 724**

30 **N-[3-(1-{3-[2-(3-CHLOROPHENYL)-1-METHYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using N-(3-{1-[5-(3-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-methyl-1-phenylhydrazine: ESMS  $m/e$ : 528.2 ( $M + H$ )<sup>+</sup>.



**Example 725**

**N-[3-(1-{3-[2-(3-CHLOROPHENYL)-1-PHENYL-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**

5 Prepared by Procedure E and Scheme M using N-(3-{1-[5-(3-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1,1-diphenylhydrazine hydrochloride: ESMS m/e: 590.3 (M + H)<sup>+</sup>.

10 **Example 726**

**N-[3-(1-{3-[2-(3-CHLOROPHENYL)-5-METHOXY-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using N-(3-{1-[5-(3-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-  
15 methylpropanamide and 4-methoxyphenylhydrazine hydrochloride: ESMS m/e: 544.3 (M + H)<sup>+</sup>.

**Example 727**

**N-[3-(1-{3-[2-(3-CHLOROPHENYL)-5-METHYL-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**

20 Prepared by Procedure E and Scheme M using N-(3-{1-[5-(3-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-methylphenylhydrazine hydrochloride: ESMS m/e: 528.2 (M + H)<sup>+</sup>.

25

**Example 728**

**N-[3-(1-{3-[2-(3-CHLOROPHENYL)-1H-BENZO[G]INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using N-(3-{1-[5-(3-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-  
30 methylpropanamide and 1-naphthylhydrazine hydrochloride: ESMS m/e: 564.2 (M + H)<sup>+</sup>.

**Example 729**

**N-[3-(1-{3-[2-(3-CHLOROPHENYL)-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using N-(3-{1-[5-(3-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and phenylhydrazine: ESMS m/e: 514.2 (M + H)<sup>+</sup>.

**Example 730**

10 **N-[3-(1-{3-[2-(2-CHLOROPHENYL)-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using N-(3-{1-[5-(2-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and phenylhydrazine: ESMS m/e: 514.2 (M + H)<sup>+</sup>.

**Example 731**

20 **N-[3-(1-{3-[2-(2-CHLOROPHENYL)-5-(TRIFLUOROMETHOXY)-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure E and Scheme M using N-(3-{1-[5-(2-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-(trifluoromethoxy)phenylhydrazine hydrochloride: ESMS m/e: 598.2 (M + H)<sup>+</sup>.

25

**Example 732**

30 **N-[3-(1-{3-[2-(2-CHLOROPHENYL)-1H-BENZO [G] INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure E and Scheme M using N-(3-{1-[5-(2-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-naphthylhydrazine hydrochloride: ESMS m/e: 564.2 (M + H)<sup>+</sup>.

**Example 733**

***N*-[3-(1-{3-[2-(2-CHLOROPHENYL)-7-METHYL-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-(2-methylphenyl)hydrazine hydrochloride: ESMS *m/e*: 528.2 (*M* + *H*)<sup>+</sup>.

**Example 734**

***N*-[3-(1-{3-[2-(2-CHLOROPHENYL)-1-PHENYL-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1,1-diphenylhydrazine hydrochloride: ESMS *m/e*: 590.2 (*M* + *H*)<sup>+</sup>.

**Example 735**

***N*-[3-(1-{3-[2-(2-CHLOROPHENYL)-1-METHYL-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-methyl-1-phenylhydrazine: ESMS *m/e*: 528.2 (*M* + *H*)<sup>+</sup>.

**Example 736**

***N*-[3-(1-{3-[2-(2-CHLOROPHENYL)-5-METHYL-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-methylphenylhydrazine hydrochloride: ESMS *m/e*: 528.2 (*M* + *H*)<sup>+</sup>.

**Example 737**

**N-[3-(1-{3-[2-(3- IODOPHENYL)-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using N-(3-{1-[5-(3-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and phenylhydrazine: ESMS  $m/e$ : 606.2 (M + H)<sup>+</sup>.

**Example 738**

**N-[3-(1-{3-[2-(3- IODOPHENYL)-1-METHYL-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using N-(3-{1-[5-(3-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-methyl-1-phenylhydrazine: ESMS  $m/e$ : 620.2 (M + H)<sup>+</sup>.

15

**Example 739**

**N-[3-(1-{3-[2-(3- IODOPHENYL)-1-PHENYL-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using N-(3-{1-[5-(3-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1,1-diphenylhydrazine hydrochloride: ESMS  $m/e$ : 682.2 (M + H)<sup>+</sup>.

20

**Example 740**

**N-[3-(1-{3-[2-(3- IODOPHENYL)-1H-BENZO[G] INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using N-(3-{1-[5-(3-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-naphthylhydrazine hydrochloride: ESMS  $m/e$ : 656.2 (M + H)<sup>+</sup>.

30

**Example 741**

***N*-[3-(1-{3-[2-(3- IODOPHENYL)-5-(TRIFLUOROMETHOXY)-1*H*-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-(trifluoromethoxy)phenylhydrazine hydrochloride: ESMS  $m/e$ : 690.2 ( $M + H$ )<sup>+</sup>.

**Example 742**

***N*-[3-(1-{3-[2-(3- IODOPHENYL)-5-METHYL-1*H*-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-methylphenylhydrazine hydrochloride: ESMS  $m/e$ : 620.2 ( $M + H$ )<sup>+</sup>.

**Example 743**

***N*-[3-(1-{3-[2-(3- IODOPHENYL)-7-METHYL-1*H*-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-(2-methylphenyl)hydrazine hydrochloride: ESMS  $m/e$ : 620.2 ( $M + H$ )<sup>+</sup>.

25

**Example 744**

***N*-[3-(1-{3-[2-(4- IODOPHENYL)-5-(TRIFLUOROMETHOXY)-1*H*-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-

(trifluoromethoxy)phenylhydrazine hydrochloride: ESMS  
 $m/e$ : 690.1 (M + H)<sup>+</sup>.

**Example 745**

5 **N-[3-(1-{3-[2-(4-iodophenyl)-5-methyl-1H-indol-3-  
 YL]propyl}-4-piperidinyl)phenyl]-2-methylpropanamide:**  
 Prepared by Procedure E and Scheme M using N-(3-{1-[5-  
 (4-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-  
 methylpropanamide and 4-methylphenylhydrazine  
 10 hydrochloride: ESMS  $m/e$ : 620.1 (M + H)<sup>+</sup>.

**Example 746**

**N-[3-(1-{3-[2-(4-iodophenyl)-7-methyl-1H-indol-3-  
 YL]propyl}-4-piperidinyl)phenyl]-2-methylpropanamide:**  
 15 Prepared by Procedure E and Scheme M using N-(3-{1-[5-  
 (4-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-  
 methylpropanamide and 1-(2-methylphenyl)hydrazine  
 hydrochloride: ESMS  $m/e$ : 620.1 (M + H)<sup>+</sup>.

**Example 747**

20 **N-[3-(1-{3-[2-(4-iodophenyl)-1-phenyl-1H-indol-3-  
 YL]propyl}-4-piperidinyl)phenyl]-2-methylpropanamide:**  
 Prepared by Procedure E and Scheme M using N-(3-{1-[5-  
 (4-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-  
 25 methylpropanamide and 1,1-diphenylhydrazine  
 hydrochloride: ESMS  $m/e$ : 682.1 (M + H)<sup>+</sup>.

**Example 748**

**N-[3-(1-{3-[2-(4-iodophenyl)-1-methyl-1H-indol-3-  
 YL]propyl}-4-piperidinyl)phenyl]-2-methylpropanamide:**  
 30 Prepared by Procedure E and Scheme M using N-(3-{1-[5-  
 (4-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-

methylpropanamide and 1-methyl-1-phenylhydrazine:  
ESMS  $m/e$ : 620.1 ( $M + H$ )<sup>+</sup>.

**Example 749**

5 ***N*-[3-(1-{3-[2-(4-iodophenyl)-1*H*-benzo[*G*]indol-3-yl]propyl}-4-piperidinyl)phenyl]-2-methylpropanamide:**  
Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-naphthylhydrazine hydrochloride:  
10 ESMS  $m/e$ : 656.1 ( $M + H$ )<sup>+</sup>.

**Example 750**

***N*-[3-(1-{3-[2-(4-iodophenyl)-1*H*-indol-3-yl]propyl}-4-piperidinyl)phenyl]-2-methylpropanamide:**  
15 Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and phenylhydrazine: ESMS  $m/e$ : 606.1 ( $M + H$ )<sup>+</sup>.

20 **Example 751**

***N*-[3-(1-{3-[2-(3-bromophenyl)-5-(trifluoromethoxy)-1*H*-indol-3-yl]propyl}-4-piperidinyl)phenyl]-2-methylpropanamide:** Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-(trifluoromethoxy)phenylhydrazine hydrochloride: ESMS  
25  $m/e$ : 642.0 ( $M + H$ )<sup>+</sup>.

**Example 752**

30 ***N*-[3-(1-{3-[2-(4-bromophenyl)-1*H*-benzo[*G*]indol-3-yl]propyl}-4-piperidinyl)phenyl]-2-methylpropanamide:**  
Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-

methylpropanamide and 1-naphthylhydrazine  
hydrochloride: ESMS  $m/e$ : 608.0 ( $M + H$ )<sup>+</sup>.

**Example 753**

5 ***N*-[3-(1-{3-[2-(4-BROMOPHENYL)-7-METHYL-1*H*-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**  
Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-(2-methylphenyl)hydrazine  
10 hydrochloride: ESMS  $m/e$ : 572 ( $M + H$ )<sup>+</sup>.

**Example 754**

***N*-[3-(1-{3-[2-(4-BROMOPHENYL)-5-(TRIFLUOROMETHOXY)-1*H*-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure E and Scheme M  
15 using *N*-(3-{1-[5-(4-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-(trifluoromethoxy)phenylhydrazine hydrochloride: ESMS  
 $m/e$ : 642 ( $M + H$ )<sup>+</sup>.

20

**Example 755**

***N*-[3-(1-{3-[2-(3-BROMOPHENYL)-1*H*-BENZO [G] INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**  
Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-naphthylhydrazine hydrochloride:  
25 ESMS  $m/e$ : 608.0 ( $M + H$ )<sup>+</sup>.

**Example 756**

30 ***N*-[3-(1-{3-[2-(4-BROMOPHENYL)-1*H*-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-



methylpropanamide and phenylhydrazine: ESMS  $m/e$ :  
558.1 (M + H)<sup>+</sup>.

**Example 757**

5 **N-[3-(1-{3-[2-(3-BROMOPHENYL)-1-PHENYL-1H-INDOL-3-  
YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:**  
Prepared by Procedure E and Scheme M using N-(3-{1-[5-  
(3-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-  
methylpropanamide and 1,1-diphenylhydrazine  
10 hydrochloride: ESMS  $m/e$ : 634.0 (M + H)<sup>+</sup>.

**Example 758**

**N-[3-(1-{3-[2-(3-BROMOPHENYL)-1-METHYL-1H-INDOL-3-  
YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:**  
15 Prepared by Procedure E and Scheme M using N-(3-{1-[5-  
(3-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-  
methylpropanamide and 1-methyl-1-phenylhydrazine: ESMS  
 $m/e$ : 572.0 (M + H)<sup>+</sup>.

**Example 759**

20 **N-[3-(1-{3-[2-(4-BROMOPHENYL)-1-METHYL-1H-INDOL-3-  
YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:**  
Prepared by Procedure E and Scheme M using N-(3-{1-[5-  
(4-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-  
25 methylpropanamide and 1-methyl-1-phenylhydrazine: ESMS  
 $m/e$ : 572.0 (M + H)<sup>+</sup>.

**Example 760**

30 **N-[3-(1-{3-[2-(4-BROMOPHENYL)-1-PHENYL-1H-INDOL-3-  
YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:**  
Prepared by Procedure E and Scheme M using N-(3-{1-[5-  
(4-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-

methylpropanamide and 1,1-diphenylhydrazine  
hydrochloride: ESMS  $m/e$ : 634.0 ( $M + H$ )<sup>+</sup>.

**Example 761**

5 **N-[3-(1-{3-[2-(4-BROMOPHENYL)-5-METHOXY-1H-INDOL-3-  
YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using N-(3-{1-[5-(4-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-methoxyphenylhydrazine  
10 hydrochloride: ESMS  $m/e$ : 588.1 ( $M + H$ )<sup>+</sup>.

**Example 762**

**N-[3-(1-{3-[2-(3-BROMOPHENYL)-7-METHYL-1H-INDOL-3-  
YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:**

15 Prepared by Procedure E and Scheme M using N-(3-{1-[5-(3-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-(2-methylphenyl)hydrazine  
hydrochloride: ESMS  $m/e$ : 572 ( $M + H$ )<sup>+</sup>.

**Example 763**

20 **N-[3-(1-{3-[2-(3-BROMOPHENYL)-5-METHYL-1H-INDOL-3-  
YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using N-(3-{1-[5-(3-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-methylphenylhydrazine  
25 hydrochloride: ESMS  $m/e$ : 572 ( $M + H$ )<sup>+</sup>.

**Example 764**

30 **N-[3-(1-{3-[2-(4-BROMOPHENYL)-5-METHYL-1H-INDOL-3-  
YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using N-(3-{1-[5-(4-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-

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methylpropanamide and 4-methylphenylhydrazine  
hydrochloride: ESMS  $m/e$ : 572.0 ( $M + H$ )<sup>+</sup>.

**Example 765**

5 N-[3-(1-{3-[2-(3-BROMOPHENYL)-5-METHOXY-1H-INDOL-3-  
YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:  
Prepared by Procedure E and Scheme M using N-(3-{1-[5-  
(3-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-  
methylpropanamide and 4-methoxyphenylhydrazine  
10 hydrochloride: ESMS  $m/e$ : 588.0 ( $M + H$ )<sup>+</sup>.

**Example 766**

2-METHYL-N-[3-(1-{3-[2-(3-NITROPHENYL)-1H-INDOL-3-  
YL] PROPYL}-4-PIPERIDINYL) PHENYL] PROPANAMIDE:  
15 Prepared by Procedure E and Scheme M using 2-methyl-N-  
(3-{1-[5-(3-nitrophenyl)-5-oxopentyl]-4-  
piperidinyl}phenyl)propanamide and phenylhydrazine: ESMS  
 $m/e$ : 525.2 ( $M + H$ )<sup>+</sup>.

20 **Example 767**

2-METHYL-N-[3-(1-{3-[2-(3-NITROPHENYL)-1H-BENZO[G]INDOL-  
3-YL] PROPYL}-4-PIPERIDINYL) PHENYL] PROPANAMIDE:  
Prepared by Procedure E and Scheme M using 2-methyl-N-  
(3-{1-[5-(3-nitrophenyl)-5-oxopentyl]-4-  
25 piperidinyl}phenyl)propanamide and 1-naphthylhydrazine  
hydrochloride: ESMS  $m/e$ : 575.1 ( $M + H$ )<sup>+</sup>.

**Example 768**

2-METHYL-N-[3-(1-{3-[2-(3-NITROPHENYL)-5-  
30 (TRIFLUOROMETHOXY)-1H-INDOL-3-YL] PROPYL}-4-  
PIPERIDINYL) PHENYL] PROPANAMIDE: Prepared by Procedure E  
and Scheme M using 2-methyl-N-(3-{1-[5-(3-nitrophenyl)-  
5-oxopentyl]-4-piperidinyl}phenyl)propanamide and 4-

(trifluoromethoxy)phenylhydrazine hydrochloride: ESMS  
 $m/e$ : 609.1 (M + H)<sup>+</sup>.

**Example 769**

5     **2-METHYL-N-[3-(1-{3-[5-METHYL-2-(3-NITROPHENYL)-1H-  
 INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL] PROPANAMIDE:**

Prepared by Procedure E and Scheme M using 2-methyl-N-  
 (3-{1-[5-(3-nitrophenyl)-5-oxopentyl]-4-  
 piperidinyl}phenyl)propanamide and 4-  
 10     methylphenylhydrazine hydrochloride: ESMS  $m/e$ : 539.2 (M  
 + H)<sup>+</sup>.

**Example 770**

15     **N-[3-(1-{3-[5-METHOXY-2-(3-NITROPHENYL)-1H-INDOL-3-  
 YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using 2-methyl-N-  
 (3-{1-[5-(3-nitrophenyl)-5-oxopentyl]-4-  
 piperidinyl}phenyl)propanamide and 4-  
 20     methoxyphenylhydrazine hydrochloride: ESMS  $m/e$ : 555.2 (M  
 + H)<sup>+</sup>.

**Example 771**

25     **2-METHYL-N-[3-(1-{3-[2-(3-NITROPHENYL)-1-PHENYL-1H-  
 INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL] PROPANAMIDE:**

Prepared by Procedure E and Scheme M using 2-methyl-N-  
 (3-{1-[5-(3-nitrophenyl)-5-oxopentyl]-4-  
 piperidinyl}phenyl)propanamide and 1,1-diphenylhydrazine  
 hydrochloride: ESMS  $m/e$ : 601.1 (M + H)<sup>+</sup>.

**Example 772**

30     **2-METHYL-N-[3-(1-{3-[1-METHYL-2-(3-NITROPHENYL)-1H-  
 INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL] PROPANAMIDE:**

Prepared by Procedure E and Scheme M using 2-methyl-N-

(3-{1-[5-(3-nitrophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)propanamide and 1-methyl-1-phenylhydrazine: ESMS  $m/e$ : 539.2 ( $M + H$ )<sup>+</sup>.

5 **Example 773**

2-METHYL-N-[3-(1-{3-[7-METHYL-2-(3-NITROPHENYL)-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL] PROPANAMIDE:

Prepared by Procedure E and Scheme M using 2-methyl-N-(3-{1-[5-(3-nitrophenyl)-5-oxopentyl]-4-

10 piperidinyl}phenyl)propanamide and 1-(2-methylphenyl)hydrazine hydrochloride: ESMS  $m/e$ : 539.2 ( $M + H$ )<sup>+</sup>.

**Example 774**

15 N-[3-(1-{3-[5-METHOXY-2-(4-NITROPHENYL)-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:

Prepared by Procedure E and Scheme M using 2-methyl-N-(3-{1-[5-(4-nitrophenyl)-5-oxopentyl]-4-

20 piperidinyl}phenyl)propanamide and 4-methoxyphenylhydrazine hydrochloride: ESMS  $m/e$ : 555.6 ( $M + H$ )<sup>+</sup>.

**Example 775**

25 N-[3-(1-{3-[2-(2-BROMOPHENYL)-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE: Prepared by

Procedure E and Scheme M using N-(3-{1-[5-(2-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and phenylhydrazine: ESMS  $m/e$ : 557.9 ( $M + H$ )<sup>+</sup>.

30

**Example 776**

2-METHYL-N-[3-(1-{3-[5-METHYL-2-(4-NITROPHENYL)-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL] PROPANAMIDE:

Prepared by Procedure E and Scheme M using 2-methyl-N-(3-{1-[5-(4-nitrophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)propanamide and 4-methylphenylhydrazine hydrochloride: ESMS  $m/e$ : 539.1 ( $M + H$ )<sup>+</sup>.

**Example 777**

2-METHYL-N-[3-(1-{3-[2-(4-NITROPHENYL)-1H-BENZO[G]INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-N-(3-{1-[5-(4-nitrophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)propanamide and 1-naphthylhydrazine hydrochloride: ESMS  $m/e$ : 574.7 ( $M + H$ )<sup>+</sup>.

**Example 778**

2-METHYL-N-(3-{1-[(5E)-5-(4-NITROPHENYL)-5-(PHENYLHYDRAZONO)PENTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE:

Prepared by Procedure E and Scheme AX using 2-methyl-N-(3-{1-[5-(4-nitrophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)propanamide and phenylhydrazine: ESMS  $m/e$ : 542.4 ( $M + H$ )<sup>+</sup>.

**Example 779**

2-METHYL-N-[3-(1-{3-[7-METHYL-2-(4-NITROPHENYL)-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE:

Prepared by Procedure E and Scheme M using 2-methyl-N-(3-{1-[5-(4-nitrophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)propanamide and 1-(2-methylphenyl)hydrazine hydrochloride: ESMS  $m/e$ : 538.8 ( $M + H$ )<sup>+</sup>.

**Example 780**

2-METHYL-N-{3-[1-((5E)-5-(4-NITROPHENYL)-5-{[4-(TRIFLUOROMETHOXY) PHENYL] HYDRAZONO}PENTYL)-4-

PIPERIDINYL] PHENYL} PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-N-(3-{1-[5-(4-nitrophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)propanamide and 4-(trifluoromethoxy)phenylhydrazine hydrochloride: ESMS  $m/e$ : 626.2 (M + H)<sup>+</sup>.

#### Example 781

N-[3-(1-{3-[2-(2-BROMOPHENYL)-1H-BENZO[G]INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:

Prepared by Procedure E and Scheme M using N-(3-{1-[5-(2-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-naphthylhydrazine hydrochloride: ESMS  $m/e$ : 608.0 (M + H)<sup>+</sup>.

#### Example 782

N-[3-(1-{3-[2-(2-BROMOPHENYL)-5-(TRIFLUOROMETHOXY)-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-

METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using N-(3-{1-[5-(2-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-(trifluoromethoxy)phenylhydrazine hydrochloride: ESMS  $m/e$ : 641.9 (M + H)<sup>+</sup>.

#### Example 783

N-[3-(1-{3-[2-(2-BROMOPHENYL)-7-METHYL-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:

Prepared by Procedure E and Scheme M using N-(3-{1-[5-(2-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-(2-methylphenyl)hydrazine hydrochloride: ESMS  $m/e$ : 572.0 (M + H)<sup>+</sup>.

**Example 784**

**N-[3-(1-{3-[2-(2-BROMOPHENYL)-1-PHENYL-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using N-(3-{1-[5-(2-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1,1-diphenylhydrazine hydrochloride: ESMS  $m/e$ : 634 (M + H)<sup>+</sup>.

**Example 785**

**N-[3-(1-{3-[2-(2-BROMOPHENYL)-5-METHYL-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using N-(3-{1-[5-(2-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-methylphenylhydrazine hydrochloride: ESMS  $m/e$ : 572.0 (M + H)<sup>+</sup>.

**Example 786**

**N-[3-(1-{3-[2-(2-IODOPHENYL)-5-(TRIFLUOROMETHOXY)-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using N-(3-{1-[5-(2-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-(trifluoromethoxy)phenylhydrazine hydrochloride: ESMS  $m/e$ : 690.0 (M + H)<sup>+</sup>.

**Example 787**

**N-[3-(1-{3-[2-(2-IODOPHENYL)-5-METHYL-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using N-(3-{1-[5-(2-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-methylphenylhydrazine hydrochloride: ESMS  $m/e$ : 620.2 (M + H)<sup>+</sup>.



**Example 788**

**2-METHYL-N-[3-(1-{3-[1-METHYL-2-(4-NITROPHENYL)-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL] PROPANAMIDE:**

5 Prepared by Procedure E and Scheme M using 2-methyl-N-(3-{1-[5-(4-nitrophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)propanamide and 1-methyl-1-phenylhydrazine: ESMS  $m/e$ : 539.6 (M + H)<sup>+</sup>.

10 **Example 789**

**2-METHYL-N-[3-(1-{3-[2-(4-NITROPHENYL)-1-PHENYL-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL] PROPANAMIDE:**

Prepared by Procedure E and Scheme M using 2-methyl-N-(3-{1-[5-(4-nitrophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)propanamide and 1,1-diphenylhydrazine hydrochloride: ESMS  $m/e$ : 601.6 (M + H)<sup>+</sup>.

15

**Example 790**

**N-[3-(1-{3-[2-(2-IODOPHENYL)-1H-INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using N-(3-{1-[5-(2-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and phenylhydrazine: ESMS  $m/e$ : 606.1 (M + H)<sup>+</sup>.

20

25

**Example 791**

**N-[3-(1-{3-[2-(2-IODOPHENYL)-1H-BENZO[G]INDOL-3-YL] PROPYL}-4-PIPERIDINYL) PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using N-(3-{1-[5-(2-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-naphthylhydrazine hydrochloride: ESMS  $m/e$ : 656.1 (M + H)<sup>+</sup>.

30

**Example 792**

**N-[3-(1-{3-[2-(2-iodophenyl)-1-phenyl-1H-indol-3-yl]propyl}-4-piperidinyl)phenyl]-2-methylpropanamide:**

Prepared by Procedure E and Scheme M using N-(3-{1-[5-(2-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1,1-diphenylhydrazine hydrochloride: ESMS  $m/e$ : 682.1 (M + H)<sup>+</sup>.

**Example 793**

**N-[3-(1-{3-[2-(2-iodophenyl)-7-methyl-1H-indol-3-yl]propyl}-4-piperidinyl)phenyl]-2-methylpropanamide:**

Prepared by Procedure E and Scheme M using N-(3-{1-[5-(2-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-(2-methylphenyl)hydrazine hydrochloride: ESMS  $m/e$ : 619.6 (M + H)<sup>+</sup>.

**Example 794**

**N-[3-(1-{3-[2-(2-bromophenyl)-1-methyl-1H-indol-3-yl]propyl}-4-piperidinyl)phenyl]-2-methylpropanamide:**

Prepared by Procedure E and Scheme M using N-(3-{1-[5-(2-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-methyl-1-phenylhydrazine: ESMS  $m/e$ : 572 (M + H)<sup>+</sup>.

**Example 795**

**4-(3,4-difluorophenyl)-N-(3-{4-[3-(isobutyrylamino)phenyl]-1-piperidinyl}propyl)-2-methyl-6-oxo-1,4,5,6-tetrahydro-3-pyridinecarboxamide:**

Prepared by Procedure AC and Scheme AM using 4-(3,4-difluorophenyl)-2-methyl-6-oxo-1,4,5,6-tetrahydro-3-pyridinecarboxylic acid and N-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS  $m/e$ : 553.0 (M + H)<sup>+</sup>.

**Example 796**

4-(2,4-DIFL

UOROPHENYL)-N-(3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-

PIPERIDINYL}PROPYL)-2-METHYL-6-OXO-1,4,5,6-TETRAHYDRO-3-

5 PYRIDINECARBOXAMIDE: Prepared by Procedure AC and  
Scheme AM using 4-(2,4-difluorophenyl)-2-methyl-6-oxo-  
1,4,5,6-tetrahydro-3-pyridinecarboxylic acid and N-{3-  
[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-  
methylpropanamide: ESMS m/e: 553.0 (M + H)<sup>+</sup>.

10

**Example 797**

N-(3-{1-[4-(4-METHOXYPHENYL)BUTYL]-4-

PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by

15 Procedure O and Scheme W using 4-(4-methoxyphenyl)-1-  
butanol and 2-methyl-N-[3-(4-  
piperidinyl)phenyl]propanamide: ESMS m/e: 409 (M + H)<sup>+</sup>.

**Example 798**

N-(4-{1-[3-(1,2-DIPHENYL-1H-INDOL-3-YL)PROPYL]-4-

20 PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure O  
and Scheme W using 3-(1,2-diphenyl-1H-indol-3-yl)-1-  
propanol and N-[4-(4-piperidinyl)phenyl]propanamide:  
ESMS m/e: 542.0 (M + H)<sup>+</sup>.

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**Example 799**

N-{4-[1-(3,3-DIPHENYLPROPYL)-4-

PIPERIDINYL}PHENYL}PROPANAMIDE: Prepared by Procedure O

and Scheme W using 3,3-diphenyl-1-propanol and

30 N-[4-(4-piperidinyl)phenyl]propanamide: ESMS m/e: 427.0  
(M + H)<sup>+</sup>.

**Example 800**

2-METHYL-N-(3-{1-[4-(4-NITROPHENYL) BUTYL]-4-  
 PIPERIDINYL}PHENYL): Prepared by Procedure O and Scheme  
 W using 4-(4-nitrophenyl)-1-butanol and 2-methyl-N-[3-  
 (4-piperidinyl)phenyl]propanamide: ESMS m/e: 424.2 (M +  
 5 H)<sup>+</sup>.

#### Example 801

2-METHYL-N-(3-{1-[2-(1-NAPHTHYL) ETHYL]-4-  
 PIPERIDINYL}PHENYL)PROPANAMIDE Prepared by Procedure O  
 10 and Scheme W using 2-(1-naphthyl)ethanol and 2-methyl-N-  
 [3-(4-piperidinyl)phenyl]propanamide: ESMS m/e: 401.2 (M  
 + H)<sup>+</sup>.

#### Example 802

15 N-{3-[1-(3,3-DIPHENYLPROPYL)-4-PIPERIDINYL]PHENYL}-2-  
 METHYLPROPANAMIDE: Prepared by Procedure O and Scheme W  
 using 3,3-diphenyl-1-propanol and 2-methyl-N-[3-(4-  
 piperidinyl)phenyl]propanamide: ESMS m/e: 441.2 (M + H)<sup>+</sup>.

#### Example 803

20 N-(3-{1-[3-(3,4-DIMETHOXYPHENYL) PROPYL]-4-  
 PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by  
 Procedure O and Scheme W using 3-(3,4-dimethoxyphenyl)-  
 1-propanol and 2-methyl-N-[3-(4-  
 25 piperidinyl)phenyl]propanamide: ESMS m/e: 425.2 (M + H)<sup>+</sup>.

#### Example 804

2-METHYL-N-{3-[1-(3-PHENYLPROPYL)-4-  
 PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure O  
 30 and Scheme W using 3-phenyl-1-propanol and  
 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  
 m/e: 365.2 (M + H)<sup>+</sup>.

**Example 805**

**2-METHYL-N-(3-{1-[3-(4-PYRIDINYL)PROPYL]-4-**

**PIPERIDINYL}PHENYL)PROPANAMIDE:** Prepared by Procedure O  
and Scheme W using 3-(4-pyridinyl)-1-propanol and 2-  
5 methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS m/e:  
366.2 (M + H)<sup>+</sup>.

**Example 806**

**N-{3-[1-(4-TERT-BUTYLBENZYL)-4-PIPERIDINYL]PHENYL}-2-**

10 **METHYLPROPANAMIDE:** Prepared by Procedure AJ and Scheme  
AV using 1-bromomethyl)-4-tert-butylbenzene and 2-  
methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS m/e:  
393.0 (M + H)<sup>+</sup>.

15 **Example 807**

**N-{3-[1-(4-BENZOYLBENZYL)-4-PIPERIDINYL]PHENYL}-2-**

**METHYLPROPANAMIDE:** Prepared by Procedure AJ and Scheme  
AV using [4-(bromomethyl)phenyl](phenyl)methanone and 2-  
methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS m/e:  
20 441.0 (M + H)<sup>+</sup>.

**1,2-DICHLORO-4-{[(1S)-3-CHLORO-1-**

**PHENYLPROPYL]OXY}BENZENE:** Prepared by Procedure A using  
3,4-dichlorophenol and (1R)-3-chloro-1-phenyl-1-  
25 propanol.

**Example 808**

**N-(3-{1-[(3S)-3-(3,4-DICHLOROPHENOXY)-3-PHENYLPROPYL]-4-**  
**PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by

30 Procedure A using 1,2-dichloro-4-{[(1S)-3-chloro-1-  
phenylpropyl]oxy}benzene and 2-methyl-N-[3-(4-  
piperidinyl)phenyl]propanamide: ESMS m/e: 525.3 (M + H)<sup>+</sup>.

**Example 809**

**N-(3-{1-[6-(2-FLUOROPHENYL)-6-HYDROXYHEXYL]-4-**

**PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by

5 Procedure L and Scheme AN using N-(3-{1-[6-(2-fluorophenyl)-6-oxohexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS  $m/e$ : 441.3 (M + H)<sup>+</sup>.

**Example 810**

10 **N-[3-(1-{5-HYDROXY-5-[4-(TRIFLUOROMETHYL)PHENYL]PENTYL}-**

**4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by

Procedure L and Scheme AN using 2-methyl-N-[3-(1-{5-oxo-5-[4-(trifluoromethyl)phenyl]pentyl}-4-

piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 477.2 (M + H)<sup>+</sup>.

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**Example 811**

**N-(3-{1-[5-(4-FLUOROPHENYL)-5-HYDROXYPENTYL]-4-**

**PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by

Procedure L and Scheme AN using N-(3-{1-[5-(4-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-

20

methylpropanamide: ESMS  $m/e$ : 427.2 (M + H)<sup>+</sup>.

**Example 812**

**N-(3-{1-[7-(2-FLUOROPHENYL)-7-HYDROXYHEPTYL]-4-**

25 **PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by

Procedure L and Scheme AN using N-(3-{1-[7-(2-fluorophenyl)-7-oxoheptyl]-4-piperidinyl}phenyl)-2-

methylpropanamide: ESMS  $m/e$ : 455.2 (M + H)<sup>+</sup>.

**Example 813**

30 **N-(3-{1-[6-(3-FLUOROPHENYL)-6-HYDROXYHEXYL]-4-**

**PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by

Procedure L and Scheme AN using N-(3-{1-[6-(3-

fluorophenyl)-6-oxohexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS  $m/e$ : 441.2 ( $M + H$ )<sup>+</sup>.

#### Example 814

5 ***N*-(3-{1-[5-(2-FLUOROPHENYL)-5-HYDROXPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure L and Scheme AN using *N*-(3-{1-[5-(2-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS  $m/e$ : 427.2 ( $M + H$ )<sup>+</sup>.

10

#### Example 815

***N*-(3-{1-[5-(3-FLUOROPHENYL)-5-HYDROXPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure L and Scheme AN using *N*-(3-{1-[5-(3-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS  $m/e$ : 427.2 ( $M + H$ )<sup>+</sup>.

15

#### Example 816

***N*-(3-{1-[5-(3-CHLOROPHENYL)-5-HYDROXPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure L and Scheme AN using *N*-(3-{1-[5-(3-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS  $m/e$ : 443.1 ( $M + H$ )<sup>+</sup>.

20

#### Example 817

***N*-(3-{1-[6-(4-FLUOROPHENYL)-6-HYDROXYHEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure L and Scheme AN using *N*-(3-{1-[6-(4-fluorophenyl)-6-oxohexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS  $m/e$ : 441.2 ( $M + H$ )<sup>+</sup>.

25

30

**Example 818**

**N-(3-{1-[6-(4-CHLOROPHENYL)-6-HYDROXYHEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure L and Scheme AN using N-(3-{1-[6-(4-chlorophenyl)-6-oxohexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS  $m/e$ : 456.9 (M + H)<sup>+</sup>.

**Example 819**

**N-(3-{1-[5-(4-CHLOROPHENYL)-5-HYDROXPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure L and Scheme AN using N-(3-{1-[5-(4-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS  $m/e$ : 443.0 (M + H)<sup>+</sup>.

**Example 820**

**N-(4-{1-[(9-ETHYL-9H-CARBAZOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)BUTANAMIDE:** Prepared by Procedure F and Scheme R, without HOAc, using 9-ethyl-9H-carbazole-3-carbaldehyde and N-[4-(4-piperidinyl)phenyl]butanamide: ESMS  $m/e$ : 454.2 (M + H)<sup>+</sup>.

**Example 821**

**N-(3-{1-[(9-ETHYL-9H-CARBAZOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE:** Prepared by Procedure F and Scheme R, without HOAc, using 9-ethyl-9H-carbazole-3-carbaldehyde and N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 440.5 (M + H)<sup>+</sup>.

**Example 822**

**N-(3-{1-[(1,9-DIMETHYL-9H-CARBAZOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure F and Scheme R, without HOAc, using 1,9-dimethyl-9H-carbazole-3-carbaldehyde and 2-methyl-N-[3-



(4-

piperidinyl)phenyl]propanamide:  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.05-6.77 (m, 10H), 5.20-5.12 (m, 1H), 4.04 (s, 3H), 3.93 (s, 2H), 3.34-3.24 (m, 2H), 2.79 (s, 3H), 2.56-2.38 (m, 2H), 2.38-2.26 (m, 2H), 2.08-1.88 (m, 2H), 1.82-1.70 (m, 2H), 1.16 (d, 6H,  $J = 6.8$  Hz); ESMS  $m/e$ : 454.2 ( $M + H$ ) $^+$ .

**Example 823**

***N*-(3-{1-[(9-ETHYL-9H-CARBAZOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE:**

Prepared by Procedure F and Scheme R, without HOAc, using 9-ethyl-9H-carbazole-3-carbaldehyde and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS  $m/e$ : 452.6 ( $M + H$ ) $^+$ .

**Example 824**

**1-(3-{1-[(9-ETHYL-9H-CARBAZOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)-2-PYRROLIDINONE:**

Prepared by Scheme R and Procedure F. A solution of 1-(9-ethyl-9H-carbazol-3-yl)ethanone (22.3 mg, 0.100 mmol) and 1-[3-(4-piperidinyl)phenyl]-2-pyrrolidinone (27.2 mg, 0.100 mmol) in 1,2-dichloroethane (1.00 mL) was treated with sodium triacetoxyborohydride (63.6 mg, 0.300 mmol) and HOAc (5.70  $\mu\text{L}$ , 0.100 mmol). The mixture was stirred overnight at room temperature. The reaction mixture was treated with a saturated aqueous  $\text{NaHCO}_3$  solution (10 mL). The aqueous layer was extracted with  $\text{CH}_2\text{Cl}_2$  (3 X 10 mL) and the combined organic layers were washed with brine (10 mL), dried over  $\text{MgSO}_4$  and concentrated in vacuo. The residue was purified by preparative TLC using 5% of  $\text{NH}_3$  (2.0 M in methanol) in  $\text{CH}_2\text{Cl}_2$  to give the desired product 1-(3-{1-[(9-ethyl-9H-carbazol-3-yl)methyl]-4-

piperidinyl}phenyl)-2-pyrrolidinone (4.60 mg, 9.43 %):  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.04 (d, 1H,  $J$  = 7.4 Hz), 7.99 (s, 1H), 7.43-7.28 (m, 5H), 6.96 (d, 1H,  $J$  = 7.4 Hz), 4.31 (q, 2H,  $J$  = 6.8 Hz), 3.77 (t, 2H,  $J$  = 7.3 Hz), 3.70 (s, 2H), 3.06 (d, 2H,  $J$  = 10.6 Hz), 2.56-2.42 (m, 3H), 2.07 (m, 4H), 1.77 (m, 4H), 1.36 (m, 3H); ESMS  $m/e$ : 452.5 ( $M + H$ ) $^+$ .

***N*-{3-[1-(1*H*-INDOL-5-YLMETHYL)-4-PIPERIDINYL]PHENYL}-2-**

**METHYLPROPANAMIDE:** Prepared by Procedure F and Scheme R, without HOAc, using 1*H*-indole-5-carbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 376.2 ( $M + H$ ) $^+$ .

**1-(4-CHLOROBUTYL)-1*H*-INDOLE:** Prepared by Procedure AH, and Scheme P using 1*H*-indole and 1-bromo-4-chlorobutane:  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.72-7.02 (m, 5H), 6.49 (d, 1H,  $J$  = 2.8 Hz), 4.13 (t, 2H,  $J$  = 6.8 Hz), 3.48 (t, 2H,  $J$  = 6.8 Hz), 2.06-1.92 (m, 2H), 1.80-1.70 (m, 2H).

20

**1-(3-CHLOROPROPYL)-1*H*-INDOLE:** Prepared by Procedure AH, and Scheme P using 1*H*-indole and 1-bromo-3-chloropropane:  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.70-7.04 (m, 5H), 6.50 (d, 1H,  $J$  = 2.8 Hz), 4.31 (t, 2H,  $J$  = 6.8 Hz), 3.42 (t, 2H,  $J$  = 6.4 Hz), 2.28-2.20 (m, 2H).

25

**Example 825**

***N*-(4-{1-[5-(1*H*-INDOL-1-YL)PENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure AH and Scheme P using 1-(5-chloropentyl)-1*H*-indole and 2-methyl-*N*-[4-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 432.3 ( $M + H$ ) $^+$ .

30

**Example 826**

***N*-(4-{1-[5-(1*H*-INDOL-1-YL)PENTYL]-4-**

5 **PIPERIDINYL}PHENYL)BUTANAMIDE:** Prepared by Procedure AH and Scheme P using 1-(5-chloropentyl)-1*H*-indole and *N*-[4-(4-piperidinyl)phenyl]butanamide: ESMS *m/e*: 432.3 (*M* + *H*)<sup>+</sup>.

**Example 827**

***N*-(4-{1-[5-(1*H*-INDOL-1-YL)PENTYL]-4-**

10 **PIPERIDINYL}PHENYL)PROPANAMIDE:** Prepared by Procedure AH and Scheme P using 1-(5-chloropentyl)-1*H*-indole and *N*-[4-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 418.2 (*M* + *H*)<sup>+</sup>.

**Example 828**

***N*-(4-{1-[6-(1*H*-INDOL-1-YL)HEXYL]-4-**

15 **PIPERIDINYL}PHENYL)PROPANAMIDE:** Prepared by Procedure AH and Scheme P using 1-(6-chlorohexyl)-1*H*-indole and *N*-[4-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 432.3 (*M* + *H*)<sup>+</sup>.

20

**Example 829**

**2-METHYL-*N*-(3-{1-[(1-METHYL-1*H*-INDOL-2-YL)METHYL]-4-**

25 **PIPERIDINYL}PHENYL)PROPANAMIDE:** Prepared by Procedure F and Scheme R, without HOAc, using 1-methyl-1*H*-indole-2-carbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 390.3 (*M* + *H*)<sup>+</sup>.

**Example 830**

30 ***N*-{3-[1-(1*H*-INDOL-4-YLMETHYL)-4-PIPERIDINYL]PHENYL}-2-**

**METHYLPROPANAMIDE:** Prepared by Procedure F and Scheme R, without HOAc, using 1*H*-indole-4-carbaldehyde and 2-

methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 376.2 ( $M + H$ )<sup>+</sup>.

### Example 831

5 *N*-(4-{1-[6-(1*H*-INDOL-1-YL)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure AH and Scheme P using 1-(6-chlorohexyl)-1*H*-indole and 2-methyl-*N*-[4-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 446.3 ( $M + H$ )<sup>+</sup>.

10

### Example 832

*N*-{3-[1-(1*H*-INDOL-7-YLMETHYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure F and Scheme R, without HOAc, using 1*H*-indole-7-carbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 376.2 ( $M + H$ )<sup>+</sup>.

15

### Example 833

*N*-[3-(1-{[1-(4-METHOXYPHENYL)-1*H*-INDOL-5-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-iodo-4-methoxybenzene and *N*-{3-[1-(1*H*-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS  $m/e$ : 482.0 ( $M + H$ )<sup>+</sup>.

25

### Example 834

METHYL 4-[4-({4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}METHYL)-1*H*-INDOL-1-YL]BENZOATE: Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using methyl 4-iodobenzoate and *N*-{3-[1-(1*H*-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS  $m/e$ : 510.3 ( $M + H$ )<sup>+</sup>.

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**Example 835**

**2-METHYL-N-[3-(1-{[1-(3-METHYLPHENYL)-1H-INDOL-5-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-iodo-3-methylbenzene and N-{3-[1-(1H-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS  $m/e$ : 466.3 (M + H)<sup>+</sup>.

**Example 836**

**N-[3-(1-{[1-(4-FLUOROPHENYL)-1H-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-fluoro-4-iodobenzene and N-{3-[1-(1H-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.66-6.92 (m, 12H), 6.65 (d, 1H, J = 3.2 Hz), 3.69 (s, 2H), 3.15-3.02 (m, 2H), 2.58-2.40 (m, 2H), 2.20-2.04 (m, 2H), 1.94-1.76 (m, 4H), 1.25 (d, 6H, J = 6.8 Hz); ESMS  $m/e$ : 470.6 (M + H)<sup>+</sup>.

**Example 837**

**N-(3-{1-[4-(1H-INDOL-1-YL)BUTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure AH and Scheme P using 1-(4-chlorobutyl)-1H-indole and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 418.3 (M + H)<sup>+</sup>.

**Example 838**

**N-[3-(1-{[1-(4-CHLOROPHENYL)-1H-INDOL-5-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-chloro-4-iodobenzene and N-{3-[1-(1H-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS  $m/e$ : 486.2 (M + H)<sup>+</sup>.

**Example 839**

***N*-[3-(1-{[1-(3-METHOXYPHENYL)-1*H*-INDOL-5-YL]METHYL}-4-**

**PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by

5 Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-iodo-3-methoxybenzene and *N*-{3-[1-(1*H*-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 482.2 (*M* + *H*)<sup>+</sup>.

**Example 840**

***N*-(4-{1-[4-(1*H*-INDOL-1-YL)BUTYL]-4-**

**PIPERIDINYL}PHENYL)BUTANAMIDE:** Prepared by Procedure AH

and Scheme P using 1-(4-chlorobutyl)-1*H*-indole and *N*-[4-

15 (4-piperidinyl)phenyl]butanamide: ESMS *m/e*: 418.2 (*M* + *H*)<sup>+</sup>.

**Example 841**

***N*-[3-(1-{[1-(2-METHOXYPHENYL)-1*H*-INDOL-5-YL]METHYL}-4-**

**PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by

20 Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-iodo-2-methoxybenzene and *N*-{3-[1-(1*H*-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide:

ESMS *m/e*: 482.2 (*M* + *H*)<sup>+</sup>.

**Example 842**

***N*-[3-(1-{[1-(3-CHLOROPHENYL)-1*H*-INDOL-5-YL]METHYL}-4-**

**PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by

25 Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-chloro-3-iodobenzene and *N*-{3-[1-(1*H*-indol-5-

30 ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide:

ESMS *m/e*: 486.2 (*M* + *H*)<sup>+</sup>.

**Example 843**

**METHYL 2-[5-({4-[3-(ISOBUTYRYLAMINO) PHENYL]-1-PIPERIDINYL}METHYL)-1H-INDOL-1-YL]BENZOATE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using methyl 2-iodobenzoate and N-{3-[1-(1H-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS  $m/e$ : 510.2 (M + H)<sup>+</sup>.

**Example 844**

**N-(3-{1-[3-(1H-INDOL-1-YL) PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure AH and Scheme P using 1-(3-chloropropyl)-1H-indole and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 404.2 (M + H)<sup>+</sup>.

**Example 845**

**2-METHYL-N-{3-[1-({1-[4-(TRIFLUOROMETHYL) PHENYL]-1H-INDOL-5-YL}METHYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-iodo-4-(trifluoromethyl)benzene and N-{3-[1-(1H-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS  $m/e$ : 520.2 (M + H)<sup>+</sup>.

**Example 846**

**N-(3-{1-[(1-[1,1'-BIPHENYL]-2-YL-1H-INDOL-5-YL)METHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 2-iodo-1,1'-biphenyl and N-{3-[1-(1H-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS  $m/e$ : 528.3 (M + H)<sup>+</sup>.

**Example 847**

2-METHYL-N-[3-(1-{[1-(2-METHYLPHENYL)-1H-INDOL-5-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-iodo-2-methylbenzene and N-{3-[1-(1H-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS m/e: 466.2 (M + H)<sup>+</sup>.

**Example 848**

2-METHYL-N-[3-(1-{[1-(4-METHYLPHENYL)-1H-INDOL-5-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-iodo-4-methylbenzene and N-{3-[1-(1H-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS m/e: 466.3 (M + H)<sup>+</sup>.

**Example 849**

N-[3-(1-{[1-(2-CHLOROPHENYL)-1H-INDOL-5-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-chloro-2-iodobenzene and N-{3-[1-(1H-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS m/e: 486.2 (M + H)<sup>+</sup>.

**Example 850**

2-METHYL-N-{3-[1-({1-[3-(TRIFLUOROMETHYL)PHENYL]-1H-INDOL-5-YL}METHYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-iodo-3-(trifluoromethyl)benzene and N-{3-[1-(1H-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.80-6.94 (m, 12H), 6.69 (d, 1H, J = 3.6 Hz), 3.36 (s, 2H), 3.10-3.00 (m, 2H), 2.58-2.42 (m, 2H), 2.16-2.02 (m, 2H),



1.85-1.75 (m, 4H), 1.25 (d, 6H,  $J = 7.2$  Hz); ESMS  $m/e$ : 520.2 ( $M + H$ )<sup>+</sup>.

#### Example 851

5 **2-METHYL-N-[3-(1-{[1-(2-NITROPHENYL)-1H-INDOL-5-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-iodo-2-nitrobenzene and N-{3-[1-(1H-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide:  
 10 ESMS  $m/e$ : 497.2 ( $M + H$ )<sup>+</sup>.

#### Example 852

**N-[3-(1-{[1-(2-FLUOROPHENYL)-1H-INDOL-5-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by  
 15 Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-fluoro-2-iodobenzene and N-{3-[1-(1H-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide:  
 ESMS  $m/e$ : 470.2 ( $M + H$ )<sup>+</sup>.

#### Example 853

20 **2-METHYL-N-[3-(1-{[1-(1-NAPHTHYL)-1H-INDOL-5-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-iodonaphthalene and N-{3-[1-(1H-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide:  
 25 ESMS  $m/e$ : 502.2 ( $M + H$ )<sup>+</sup>.

#### Example 854

30 **N-[3-(1-{[1-(2,3-DICHLOROPHENYL)-1H-INDOL-5-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1,2-dichloro-3-iodobenzene and N-{3-[1-(1H-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: <sup>1</sup>H

NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.68-6.94 (m, 12H), 6.68 (d, 1H, J = 2.8 Hz), 3.69 (s, 2H), 3.15-3.02 (m, 2H), 2.54-2.42 (m, 2H), 2.18-2.02 (m, 2H), 1.88-1.76 (m, 4H), 1.25 (d, 6H, J = 6.8 Hz); ESMS m/e: 520.1 (M + H)<sup>+</sup>.

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**Example 855**

**N-[3-(1-{[1-(2,3-DICHLOROPHENYL)-1H-INDOL-7-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1,2-dichloro-3-iodobenzene and N-{3-[1-(1H-indol-7-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS m/e: 520.2 (M + H)<sup>+</sup>.

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**Example 856**

**N-[3-(1-{[1-(3-METHOXYPHENYL)-1H-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-iodo-3-methoxybenzene and N-{3-[1-(1H-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS m/e: 482.3 (M + H)<sup>+</sup>.

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**Example 857**

**N-[3-(1-{[1-(2,3-DICHLOROPHENYL)-1H-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1,2-dichloro-3-iodobenzene and N-{3-[1-(1H-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS m/e: 520.2 (M + H)<sup>+</sup>.

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**Example 858**

**N-[3-(1-{[1-(3-CHLOROPHENYL)-1H-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu,

465

using 1-chloro-3-iodobenzene and *N*-{3-[1-(1*H*-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 486.2 (*M* + *H*)<sup>+</sup>.

5      **Example 859**

2-METHYL-*N*-[3-(1-{[1-(3-METHYLPHENYL)-1*H*-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-iodo-3-methylbenzene and *N*-{3-[1-(1*H*-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide:  
10      ESMS *m/e*: 466.3 (*M* + *H*)<sup>+</sup>.

**Example 860**

15      *N*-[3-(1-{[1-(3-METHOXYPHENYL)-1*H*-INDOL-7-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-iodo-3-methoxybenzene and *N*-{3-[1-(1*H*-indol-7-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide:  
ESMS *m/e*: 482.3 (*M* + *H*)<sup>+</sup>.

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**Example 861**

2-METHYL-*N*-{3-[1-({1-[3-(TRIFLUOROMETHYL)PHENYL]-1*H*-INDOL-4-YL}METHYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-iodo-3-(trifluoromethyl)benzene and  
25      *N*-{3-[1-(1*H*-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 520.2 (*M* + *H*)<sup>+</sup>.

**Example 862**

30      *N*-[3-(1-{[1-(3,4-DIMETHYLPHENYL)-1*H*-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using  
*N*-{3-[1-(1*H*-indol-4-ylmethyl)-4-

piperidinyl]phenyl}-2-methylpropanamide and 4-iodo-1,2-dimethylbenzene: ESMS  $m/e$ : 480.0 ( $M + H$ )<sup>+</sup>.

#### Example 863

5 ***N*-[3-(1-{[1-(3,4-DIFLUOROPHENYL)-1*H*-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1,3-dichloro-5-iodobenzene and *N*-{3-[1-(1*H*-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide:  
10 ESMS  $m/e$ : 520.0 ( $M + H$ )<sup>+</sup>.

#### Example 864

***N*-[3-(1-{[1-(3,4-DICHLOROPHENYL)-1*H*-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by  
15 Procedure C and Scheme Q1, with CuBr in place of Cu, using 1,2-dichloro-4-iodobenzene and *N*-{3-[1-(1*H*-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide:  
ESMS  $m/e$ : 520.0 ( $M + H$ )<sup>+</sup>.

#### Example 865

20 ***N*-[3-(1-{[1-(2-CHLORO-4-FLUOROPHENYL)-1*H*-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:**  
Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 2-chloro-4-fluoro-1-iodobenzene and  
25 *N*-{3-[1-(1*H*-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS  $m/e$ : 504.0 ( $M + H$ )<sup>+</sup>.

#### Example 866

30 ***N*-[3-(1-{[1-(2,4-DIFLUOROPHENYL)-1*H*-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 2,4-difluoro-1-iodobenzene and *N*-{3-[1-(1*H*-indol-

4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS  $m/e$ : 488.0 (M + H)<sup>+</sup>.

#### Example 867

5 2-METHYL-N-[3-(1-{[1-(3-PYRIDINYL)-1H-INDOL-7-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 3-iodopyridine and N-{3-[1-(1H-indol-7-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS  $m/e$ :  
10 453.1 (M + H)<sup>+</sup>.

#### Example 868

N-{3-[1-(1H-INDOL-6-YLMETHYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure F and Scheme R  
15 using 1H-indole-6-carbaldehyde and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 376.2 (M + H)<sup>+</sup>.

#### Example 869

20 2-METHYL-N-[3-(1-{[1-(4-PYRIDINYL)-1H-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 4-iodopyridine and N-{3-[1-(1H-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS  $m/e$ :  
25 453.2 (M + H)<sup>+</sup>.

#### Example 870

2-METHYL-N-[3-(1-{[1-(2-PYRIDINYL)-1H-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared  
30 by Procedure C and Scheme Q1, with CuBr in place of Cu, using 2-iodopyridine and N-{3-[1-(1H-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS  $m/e$ :  
453.2 (M + H)<sup>+</sup>.

**Example 871**

**N-[3-(1-{[1-(2-FLUOROPHENYL)-1H-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-fluoro-2-iodobenzene and N-{3-[1-(1H-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide:  
 5 ESMS m/e: 470.1 (M + H)<sup>+</sup>.

**Example 872**

**N-[3-(1-{[1-(4-CHLOROPHENYL)-1H-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-chloro-4-iodobenzene and N-{3-[1-(1H-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide:  
 10  
 15 ESMS m/e: 486.1 (M + H)<sup>+</sup>.

**Example 873**

**2-METHYL-N-[3-(1-{[1-(3-PYRIDINYL)-1H-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 3-iodopyridine and N-{3-[1-(1H-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS m/e:  
 20  
 453.2 (M + H)<sup>+</sup>.

**Example 874**

**N-[3-(1-{[1-(2,3-DIMETHYLPHENYL)-1H-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-iodo-2,3-dimethylbenzene and N-{3-[1-(1H-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide:  
 25  
 30 ESMS m/e: 480.1 (M + H)<sup>+</sup>.

**Example 875**

**N-[3-(1-{[1-(3-FLUOROPHENYL)-1H-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-fluoro-3-iodobenzene and N-{3-[1-(1H-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS m/e: 470.1 (M + H)<sup>+</sup>.

**Example 876**

**2-METHYL-N-{3-[1-({1-[2-(TRIFLUOROMETHYL)PHENYL]-1H-INDOL-4-YL}METHYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-iodo-2-(trifluoromethyl)benzene and N-{3-[1-(1H-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS m/e: 520.1 (M + H)<sup>+</sup>.

**Example 877**

**N-[3-(1-{[1-(2-CHLOROPHENYL)-1H-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-chloro-2-iodobenzene and N-{3-[1-(1H-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS m/e: 486.1 (M + H)<sup>+</sup>.

**Example 878**

**N-[3-(1-{[1-(2,3-DIMETHYLPHENYL)-1H-INDOL-7-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-iodo-2,3-dimethylbenzene and N-{3-[1-(1H-indol-7-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS m/e: 480.0 (M + H)<sup>+</sup>.

2-METHYL-N-[3-(1-{5-OXO-5-

[4-

(TRIFLUOROMETHYL) PHENYL] PENTYL]-4-

PIPERIDINYL) PHENYL] PROPANAMIDE: Prepared by Procedure K  
and Scheme E using 5-chloro-1-[4-  
5 (trifluoromethyl)phenyl]-1-pentanone and 2-methyl-N-[3-  
(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 475.1 ( $M + H$ )<sup>+</sup>.

N-(3-{1-[5-(4-FLUOROPHENYL)-5-OXOPENTYL]-4-

10 PIPERIDINYL} PHENYL) -2-METHYLPROPANAMIDE: Prepared by  
Procedure K and Scheme E using 5-chloro-1-(4-  
fluorophenyl)-1-pentanone and 2-methyl-N-[3-(4-  
piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 425.2 ( $M + H$ )<sup>+</sup>.

15 N-(3-{1-[5-(3-FLUOROPHENYL)-5-OXOPENTYL]-4-

PIPERIDINYL} PHENYL) -2-METHYLPROPANAMIDE: Prepared by  
Procedure K and Scheme E using 5-chloro-1-(3-  
fluorophenyl)-1-pentanone and 2-methyl-N-[3-(4-  
piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 425.2 ( $M + H$ )<sup>+</sup>.

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N-(3-{1-[5-(3-CHLOROPHENYL)-5-OXOPENTYL]-4-

PIPERIDINYL} PHENYL) -2-METHYLPROPANAMIDE: Prepared by  
Procedure K and Scheme E using 5-chloro-1-(3-  
chlorophenyl)-1-pentanone and 2-methyl-N-[3-(4-  
25 piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 441.1 ( $M + H$ )<sup>+</sup>.

N-(3-{1-[5-(4-CHLOROPHENYL)-5-OXOPENTYL]-4-

PIPERIDINYL} PHENYL) -2-METHYLPROPANAMIDE: Prepared by  
Procedure K and Scheme E using 5-chloro-1-(4-  
30 chlorophenyl)-1-pentanone and 2-methyl-N-[3-(4-  
piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 441.1 ( $M + H$ )<sup>+</sup>.



**Example 879**

**2-METHYL-N-{3-[1-(3-OXO-3-PHENYLPROPYL)-4-**

**PIPERIDINYL}PHENYL}PROPANAMIDE:** Prepared by Procedure K and Scheme E using  $K_2CO_3$  instead of  $Na_2CO_3$  and NaI instead of KI and 3-chloro-1-phenyl-1-propanone and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 379.3 ( $M + H$ )<sup>+</sup>.

**Example 880**

**N-(3-{1-[7-(2-FLUOROPHENYL)-7-OXOHEPTYL]-4-**

**PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure K and Scheme E using  $K_2CO_3$  instead of  $Na_2CO_3$  and NaI instead of KI and 7-chloro-1-(2-fluorophenyl)-1-heptanone and 2-methyl-N-[3-(4-

piperidinyl)phenyl]propanamide:  $^1H$  NMR (400 MHz,  $CDCl_3$ ),  $\delta$  8.17 (s, br, 1H), 8.06-6.88 (m, 8H), 3.08-2.94 (m, 4H), 2.62-2.48 (m, 1H), 2.48-2.38 (m, 1H), 2.38-2.15 (m, 2H), 2.02-1.92 (m, 2H), 1.84-1.77 (m, 4H), 1.77-1.66 (m, 2H), 1.62-1.46 (m, 2H), 1.46-1.29 (m, 4H), 1.21 (d, 6H,  $J = 6.8$  Hz); ESMS  $m/e$ : 453.2 ( $M + H$ )<sup>+</sup>.

**Example 881**

**N-(3-{1-[5-(2-FLUOROPHENYL)-5-OXOPENTYL]-4-**

**PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure K and Scheme E using  $K_2CO_3$  instead of  $Na_2CO_3$  and NaI instead of KI and 5-chloro-1-(2-fluorophenyl)-1-pentanone and 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 425.2 ( $M + H$ )<sup>+</sup>.

**Example 882**

**N-(3-{1-[6-(3-FLUOROPHENYL)-6-OXOHXYL]-4-**

**PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure K and Scheme E using  $K_2CO_3$  instead of  $Na_2CO_3$  and

NaI instead of KI and 6-chloro-1-(3-fluorophenyl)-  
1-hexanone and 2-methyl-N-[3-(4-  
piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 439.2 ( $M + H$ )<sup>+</sup>.

5           **Example 883**

***N*-(3-{1-[6-(2-FLUOROPHENYL)-6-OXOHXYL]-4-  
PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by  
Procedure K and Scheme E using  $K_2CO_3$  instead of  $Na_2CO_3$  and  
NaI instead of KI and 6-chloro-1-(2-fluorophenyl)-1-  
10 hexanone and 2-methyl-N-[3-(4-  
piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 439.2 ( $M + H$ )<sup>+</sup>.

**Example 884**

***N*-(3-{1-[7-(4-FLUOROPHENYL)-7-OXOHEPTYL]-4-  
PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by  
15 Procedure K and Scheme E using  $K_2CO_3$  instead of  $Na_2CO_3$  and  
NaI instead of KI and 7-chloro-1-(4-fluorophenyl)-1-  
heptanone and 2-methyl-N-[3-(4-  
piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 453.2 ( $M + H$ )<sup>+</sup>.

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**Example 885**

***N*-(3-{1-[6-(4-CHLOROPHENYL)-6-OXOHXYL]-4-  
PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by  
Procedure K and Scheme E using  $K_2CO_3$  instead of  $Na_2CO_3$  and  
25 NaI instead of KI and 6-chloro-1-(4-chlorophenyl)-1-  
hexanone and 2-methyl-N-[3-(4-  
piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 455.1 ( $M + H$ )<sup>+</sup>.

**Example 886**

30 ***N*-(3-{1-[7-(4-CHLOROPHENYL)-7-OXOHEPTYL]-4-  
PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by  
Procedure K and Scheme E using  $K_2CO_3$  instead of  $Na_2CO_3$  and  
NaI instead of KI and 7-chloro-1-(4-chlorophenyl)-1-

heptanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 469.1 ( $M + H$ )<sup>+</sup>.

#### Example 887

5 *N*-(3-{1-[6-(4-FLUOROPHENYL)-6-OXOHEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure K and Scheme E using K<sub>2</sub>CO<sub>3</sub> instead of Na<sub>2</sub>CO<sub>3</sub> and NaI instead of KI and 6-chloro-1-(4-fluorophenyl)-1-hexanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS  $m/e$ : 439.1 ( $M + H$ )<sup>+</sup>.

#### Example 888

15 *N*-(3-{1-[6-(3-ACETYLPHENOXY)-6-(2-FLUOROPHENYL)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using 1-(3-hydroxyphenyl)ethanone and *N*-(3-{1-[6-(2-fluorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS  $m/e$ : 559.5 ( $M + H$ )<sup>+</sup>.

#### 20 Example 889

*N*-(3-{1-[6-(2-FLUOROPHENOXY)-6-(2-FLUOROPHENYL)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using 2-fluorophenol and *N*-(3-{1-[6-(2-fluorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS  $m/e$ : 535.1 ( $M + H$ )<sup>+</sup>.

#### Example 890

30 *N*-(3-{1-[6-(4-FLUOROPHENOXY)-6-(2-FLUOROPHENYL)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using 4-fluorophenol and *N*-(3-{1-[6-(2-fluorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: <sup>1</sup>H NMR (400 MHz,

CDCl<sub>3</sub>), HCl salt  $\delta$  7.72- 6.72 (m, 12H), 5.42-5.34 (m, 1H), 3.68-3.58 (m, br, 2H), 3.02-2.92 (m, 2H), 2.80-2.46 (m, 6H), 2.05-1.78 (m, 6H), 1.68-1.56 (m, 1H), 1.56-1.38 (m, 3H), 1.25 (d, 6H, J = 6.8 Hz); ESMS m/e: 535.1 (M + H)<sup>+</sup>.

#### Example 891

**N-(3-{1-[6-(2-FLUOROPHENYL)-6-(2-METHOXYPHENOXY)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 2-methoxyphenol and N-(3-{1-[6-(2-fluorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS m/e: 547.0 (M + H)<sup>+</sup>.

#### Example 892

**N-(3-{1-[6-(2-FLUOROPHENYL)-6-(4-METHOXYPHENOXY)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 4-methoxyphenol and N-(3-{1-[6-(2-fluorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS m/e: 547.1 (M + H)<sup>+</sup>.

#### Example 893

**N-(3-{1-[6-(4-ACETYLPHENOXY)-6-(2-FLUOROPHENYL)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 1-(4-hydroxyphenyl)ethanone and N-(3-{1-[6-(2-fluorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS m/e: 559.2 (M + H)<sup>+</sup>.

#### Example 894

**N-(3-{1-[6-(3,4-DIMETHOXYPHENOXY)-6-(2-FLUOROPHENYL)HEXYL]-4-PIPERIDINYL}PHENYL)-2-**

**METHYLPROPANAMIDE:**

Prepared by Procedure A and Scheme AN using 3,4-dimethoxyphenol and N-(3-{1-[6-(2-fluorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS  $m/e$ : 577.6 ( $M + H$ )<sup>+</sup>.

5

**Example 895**

**N-(3-{1-[6-(2-ETHOXYPHENOXY)-6-(2-FLUOROPHENYL)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 2-ethoxyphenol and N-(3-{1-[6-(2-fluorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS  $m/e$ : 561.1 ( $M + H$ )<sup>+</sup>.

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**Example 896**

**N-(3-{1-[6-(4-BROMOPHENOXY)-6-PHENYLHEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 4-bromophenol and N-{3-[1-(6-hydroxy-6-phenylhexyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS  $m/e$ : 577.0 ( $M + H$ )<sup>+</sup>.

15

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**Example 897**

**N-(3-{1-[6-(4-FLUOROPHENOXY)-6-(4-FLUOROPHENYL)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 4-fluorophenol and N-(3-{1-[6-(4-fluorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), HCl salt  $\delta$  8.22 (s, br, 1H), 7.74-6.70 (m, 12H), 5.05-4.94 (m, 1H), 3.66-3.52 (m, br, 2H), 3.02-2.83 (m, br, 2H), 2.81-2.58 (m, br, 4H), 2.58-2.36 (m, br, 2H), 2.02-1.66 (m, br, 6H), 1.66-1.46 (m, br, 1H), 1.46-1.35 (m, br, 3H), 1.26 (d, 6H,  $J = 6.0$  Hz); ESMS  $m/e$ : 535.1 ( $M + H$ )<sup>+</sup>.

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**Example 898**

***N*-(3-{1-[6-(4-METHOXYPHENOXY)-6-PHENYLHEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:**

Prepared by Procedure A and Scheme AN using 4-methoxyphenol and *N*-(3-{3-[1-(6-hydroxy-6-phenylhexyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 529.6 (*M* + *H*)<sup>+</sup>.

**Example 899**

***N*-(3-{1-[6-(4-CHLOROPHENOXY)-6-(4-CHLOROPHENYL)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:**

Prepared by Procedure A and Scheme AN using 4-chlorophenol and *N*-(3-{1-[6-(4-chlorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 566.9 (*M* + *H*)<sup>+</sup>.

**Example 900**

***N*-(3-{1-[6-(4-BROMOPHENOXY)-6-(4-FLUOROPHENYL)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:**

Prepared by Procedure A and Scheme AN using 4-bromophenol and *N*-(3-{1-[6-(4-fluorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 595.0 (*M* + *H*)<sup>+</sup>.

**Example 901**

***N*-(3-{1-[6-(4-CHLOROPHENOXY)-6-(4-FLUOROPHENYL)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:**

Prepared by Procedure A and Scheme AN using 4-chlorophenol and *N*-(3-{1-[6-(4-fluorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), HCl salt δ 7.93 (s, 1H), 7.72-6.68 (m, 12H), 5.06-4.98 (m, 1H), 3.66-3.50 (m, br, 2H), 3.02-2.82 (m, br, 2H), 2.80-2.57 (m, br, 4H), 2.57-2.38 (m, br, 2H), 2.02-1.76 (m, br, 6H), 1.64-1.48 (m, br, 1H), 1.48-1.36

(m, br, 3H), 1.25 (d, 6H,  $J = 6.8$  Hz); Anal. Calc. for  $C_{33}H_{41}Cl_2FN_2O_2 \cdot 0.5EtOAc$ : C, 66.55; H, 7.18; N, 4.43; Found: C, 66.35; H, 6.86; N, 4.46. ESMS  $m/e$ : 550.8 ( $M + H$ )<sup>+</sup>.

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#### Example 902

***N*-(3-{1-[6-(4-CHLOROPHENYL)-6-(4-FLUOROPHENOXY)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 4-fluorophenol and *N*-(3-{1-[6-(4-chlorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), HCl salt  $\delta$  8.22 (s, br, 1H), 7.74-6.68 (m, 12H), 5.04-4.92 (m, 1H), 3.66-3.50 (m, br, 2H), 3.00-2.82 (br, 2H), 2.80-2.58 (m, br, 4H), 2.58-2.40 (m, br, 2H), 2.00-1.68 (m, br, 6H), 1.66-1.46 (m, br, 1H), 1.46-1.36 (br, 3H), 1.25 (d, 6H,  $J = 7.2$  Hz); ESMS  $m/e$ : 551.1 ( $M + H$ )<sup>+</sup>.

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#### Example 903

***N*-(3-{1-[6-(3-ACETYLPHENOXY)-6-PHENYLHEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 1-(3-hydroxyphenyl)ethanone and *N*-{3-[1-(6-hydroxy-6-phenylhexyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS  $m/e$ : 541.2 ( $M + H$ )<sup>+</sup>.

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#### Example 904

***N*-(3-{1-[6-(4-CHLOROPHENOXY)-6-PHENYLHEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 4-chlorophenol and *N*-{3-[1-(6-hydroxy-6-phenylhexyl)-4-piperidinyl]phenyl}-2-methylpropanamide: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), HCl salt  $\delta$  8.28 (s, 1H), 7.78-6.70 (m, 13H), 5.08-4.98 (m, 1H), 3.64-3.46 (m, br, 2H), 3.02-2.82 (br, 2H), 2.82-2.56 (m,

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br, 4H), 2.56-2.34 (m, br, 2H), 2.05-1.75 (m, br, 6H), 1.64-1.48 (m, br, 1H), 1.48-1.34 (br, 3H), 1.25 (d, 6H, J = 6.8 Hz); ESMS  $m/e$ : 533.1 (M + H)<sup>+</sup>.

5                   **Example 905**

**N-(3-{1-[6-(4-BROMOPHENOXY)-6-(4-CHLOROPHENYL)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 4-bromophenol and N-(3-{1-[6-(4-chlorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS  $m/e$ : 611.0 (M + H)<sup>+</sup>.

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**Example 906**

**N-(3-{1-[6-(4-CHLOROPHENYL)-6-(4-METHOXYPHENOXY)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 4-methoxyphenol and N-(3-{1-[6-(4-chlorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS  $m/e$ : 563.1 (M + H)<sup>+</sup>.

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**Example 907**

**N-(3-{1-[6-(4-FLUOROPHENYL)-6-(4-METHOXYPHENOXY)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 4-methoxyphenol and N-(3-{1-[6-(4-fluorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), HCl salt δ 8.11 (s, 1H), 7.65-6.84 (m, 12H), 5.21-5.10 (m, 1H), 3.66-3.56 (m, br, 2H), 3.02-2.82 (br, 2H), 2.82-2.56 (m, br, 4H), 2.54 (s, 3H), 2.53-2.32 (m, br, 2H), 2.02-1.70 (m, br, 6H), 1.64-1.48 (m, br, 1H), 1.48-1.34 (br, 3H), 1.25 (d, 6H, J = 6.8 Hz); ESMS  $m/e$ : 547.1 (M + H)<sup>+</sup>.

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**Example 908**

***N*-(3-{1-[6-(3-ACETYLPHENOXY)-6-(4-FLUOROPHENYL)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 1-(3-hydroxyphenyl)ethanone and *N*-(3-{1-[6-(4-fluorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 559.1 (*M* + *H*)<sup>+</sup>.

**Example 909**

***N*-(3-{1-[6-(4-FLUOROPHENOXY)-6-PHENYLHEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 4-fluorophenol and *N*-(3-{1-[6-(6-hydroxy-6-phenylhexyl)-4-piperidinyl]phenyl}-2-methylpropanamide: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), HCl salt δ 8.05 (s, br, 1H), 7.72-6.70 (m, 13H), 5.06-4.96 (m, 1H), 3.66-3.51 (m, 2H), 3.01-2.82 (m, br, 2H), 2.82-2.57 (m, br, 4H), 2.57-2.34 (m, br, 2H), 2.05-1.78 (m, br, 6H), 1.64-1.52 (m, br, 1H), 1.52-1.16 (m, br, 3H), 1.25 (d, 6H, *J* = 7.2 Hz); ESMS *m/e*: 517.0 (*M* + *H*)<sup>+</sup>.

**Example 910**

***N*-(3-{1-[6-(2-ACETYLPHENOXY)-6-(2-FLUOROPHENYL)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 1-(2-hydroxyphenyl)ethanone and *N*-(3-{1-[6-(2-fluorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 559.0 (*M* + *H*)<sup>+</sup>.

**Example 911**

***N*-(3-{1-[6-(4-FLUOROPHENYL)-6-[2-FLUORO-5-(TRIFLUOROMETHYL)PHENOXY]HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 2-fluoro-5-(trifluoromethyl)phenol and *N*-(3-{1-

[6-(4-fluorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), HCl salt δ 8.23 (s, br, 1H), 7.74-6.88 (m, 11H), 5.20-5.12 (m, 1H), 3.68-3.52 (m, br, 2H), 3.02-2.82 (m, br, 2H), 2.82-2.60 (m, 4H), 2.58-2.38 (m, br, 2H), 2.12-2.02 (m, br, 1H), 2.02-1.80 (m, br, 5H), 1.68-1.52 (m, br, 1H), 1.52-1.36 (br, 3H), 1.25 (d, 6H, J = 7.2 Hz) ; ESMS m/e: 603.3 (M + H)<sup>+</sup>.

#### 10                    Example 912

**N-(3-{1-[6-(3-ACETYLPHENOXY)-6-(4-CHLOROPHENYL)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 1-(3-hydroxyphenyl)ethanone and N-(3-{1-[6-(4-chlorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), HCl salt δ 8.41 (s, 1H), 7.72-6.84 (m, 12H), 5.18-5.10 (m, 1H), 3.62-3.50 (m, br, 2H), 3.00-2.92 (m, 2H), 2.90-2.58 (m, 4H), 2.54 (s, 3H), 2.50-2.12 (m, 2H), 2.02-1.70 (m, br, 6H), 1.64-1.50 (m, br, 1H), 1.50-1.14 (m, br, 3H), 1.25 (d, 6H, J = 6.8 Hz); ESMS m/e: 575.3 (M + H)<sup>+</sup>.

#### Example 913

**N-[3-(1-{6-(2-FLUOROPHENYL)-6-[2-FLUORO-5-(TRIFLUOROMETHYL)PHENOXY]HEXYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 2-fluoro-5-(trifluoromethyl)phenol and N-(3-{1-[6-(2-fluorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), HCl salt δ 8.35 (s, 1H), 7.68-6.82 (m, 11H), 5.58-5.48 (m, 1H), 3.64-3.50 (m, 2H), 3.01-2.94 (m, br, 2H), 2.92-2.54 (m, 4H), 2.48-2.32 (m, br, 2H), 2.20-2.04 (m, 1H), 2.01-1.80 (m, 5H), 1.70-1.54 (m, 1H), 1.54-1.36

(m, 3H), 1.25 (d, 6H,  $J = 7.2$  Hz). Anal. Calc. for  $C_{34}H_{40}ClF_5N_2O_2 \cdot 0.6MeOH$ : C, 63.12; H, 6.49; N, 4.25; Found: C, 63.38; H, 6.61; N, 3.95. ESMS  $m/e$ : 603.3 ( $M + H$ )<sup>+</sup>.

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**Example 914**

**N-[3-(1-{6-(4-CHLOROPHENYL)-6-[2-FLUORO-5-(TRIFLUOROMETHYL)PHENOXY]HEXYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 2-fluoro-5-(trifluoromethyl)phenol and N-(3-{1-[6-(4-chlorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS  $m/e$ : 619.2 ( $M + H$ )<sup>+</sup>.

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**Example 915**

**N-[3-(1-{6-(3-FLUOROPHENYL)-6-[2-FLUORO-5-(TRIFLUOROMETHYL)PHENOXY]HEXYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 2-fluoro-5-(trifluoromethyl)phenol and N-(3-{1-[6-(3-fluorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS  $m/e$ : 603.3 ( $M + H$ )<sup>+</sup>.

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**Example 916**

**N-[3-(1-{6-[2-FLUORO-5-(TRIFLUOROMETHYL)PHENOXY]-6-PHENYLHEXYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 2-fluoro-5-(trifluoromethyl)phenol and N-{3-[1-(6-hydroxy-6-phenylhexyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS  $m/e$ : 585.3 ( $M + H$ )<sup>+</sup>.

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**Example 917**

**N-[3-(1-{7-(2-FLUOROPHENYL)-7-[2-FLUORO-5-(TRIFLUOROMETHYL)PHENOXY]HEPTYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme

AN using 2-fluoro-5-(trifluoromethyl)phenol and N-(3-{1-[7-(2-fluorophenyl)-7-hydroxyheptyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS m/e: 617.3 (M + H)<sup>+</sup>.

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#### Example 918

N-(3-{1-[5-(4-FLUOROPHENYL)-5-(4-METHOXYPHENOXY)PENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using 4-methoxyphenol and N-(3-{1-[5-(4-fluorophenyl)-5-hydroxypentyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS m/e: 533.1 (M + H)<sup>+</sup>.

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#### Example 919

N-(3-{1-[5-(4-BROMOPHENOXY)-5-(4-FLUOROPHENYL)PENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using 4-bromophenol and N-(3-{1-[5-(4-fluorophenyl)-5-hydroxypentyl]-4-piperidinyl}phenyl)-2-methylpropanamide: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), HCl salt δ 7.94 (s, br, 1H), 7.68-6.64 (m, 12H), 5.12-5.04 (m, 1H), 3.68-3.52 (m, br, 2H), 3.01-2.82 (br, 2H), 2.78-2.58 (m, br, 4H), 2.57-2.38 (m, br, 2H), 2.05-1.80 (m, br, 6H), 1.64-1.38 (m, br, 2H), 1.25 (d, 6H, J = 7.2 Hz); ESMS m/e: 581.0 (M + H)<sup>+</sup>.

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#### Example 920

N-(3-{1-[5-(4-CHLOROPHENOXY)-5-(4-CHLOROPHENYL)PENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using 4-chlorophenol and N-(3-{1-[5-(4-chlorophenyl)-5-hydroxypentyl]-4-piperidinyl}phenyl)-2-methylpropanamide: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), HCl salt δ 7.86 (s, br, 1H), 7.62-6.72 (m, 12H), 5.12-5.02 (m, 1H), 3.68-3.52 (m, br, 2H), 3.02-2.82 (br, 2H), 2.82-2.56 (m, br, 4H), 2.56-2.40 (m, br, 2H), 2.06-

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1.80 (m, br, 6H), 1.64-1.40 (m, br, 2H), 1.25 (d, 6H,  $J = 6.8$  Hz). Anal. Calc. for  $C_{32}H_{39}Cl_3N_2O_2 \cdot 1.3MeOH$ : C, 63.25; H, 7.07; N, 4.42; Found: C, 63.41; H, 6.99; N, 4.17. ESMS  $m/e$ : 553.0 ( $M + H$ )<sup>+</sup>.

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**Example 921**

***N*-(3-{1-[5-(4-CHLOROPHENOXY)-5-PHENYLPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:**

Prepared by Procedure A and Scheme AN using 4-chlorophenol and *N*-(3-

{1-(5-hydroxy-5-phenylpentyl)-4-piperidinyl}phenyl)-2-

10 methylpropanamide: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), HCl salt  $\delta$  7.72-6.72 (m, 13H), 5.12-5.04 (m, 1H), 3.66-3.52 (m, br, 2H), 3.01-2.83 (br, 2H), 2.68-2.62 (m, br, 2H), 2.62-2.48 (m, br, 4H), 2.04-1.82 (m, br, 6H), 1.62-1.40 (m, br, 2H), 1.25 (d, 6H,  $J = 7.2$  Hz); ESMS  $m/e$ : 519.1 ( $M + H$ )<sup>+</sup>.

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**Example 922**

***N*-(3-{1-[5-(3-ACETYLPHENOXY)-5-(4-FLUOROPHENYL)PENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:**

Prepared by

20 Procedure A and Scheme AN using 1-(3-hydroxyphenyl)ethanone and *N*-(3-{1-[5-(4-fluorophenyl)-5-hydroxypentyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS  $m/e$ : 545.1 ( $M + H$ )<sup>+</sup>.

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**Example 923**

***N*-(3-{1-[5-(4-CHLOROPHENYL)-5-(4-FLUOROPHENOXY)PENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:**

Prepared by Procedure A and Scheme AN using 4-fluorophenol and *N*-(3-

{1-[5-(4-chlorophenyl)-5-hydroxypentyl]-4-

30 piperidinyl}phenyl)-2-methylpropanamide: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), HCl salt  $\delta$  8.05 (s, br, 1H), 7.74-6.68 (m, 12H), 5.08-4.99 (m, 1H), 3.67-3.56 (m, br, 2H), 3.02-2.82 (br, 2H), 2.80-2.57 (m, br, 4H), 2.57-2.38 (m, br, 2H), 2.05-

1.80 (m, br, 6H), 1.64-1.40 (m, br, 2H), 1.25 (d, 6H,  $J = 7.2$  Hz). Anal. Calc. for  $C_{32}H_{39}Cl_2FN_2O_2 \cdot 1.3EtOAc$ : C, 64.93; H, 7.24; N, 4.07. Found: C, 65.01; H, 6.97; N, 3.85. ESMS  $m/e$ : 537.1 ( $M + H$ )<sup>+</sup>.

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#### Example 924

***N*-(3-{1-[5-(4-BROMOPHENOXY)-5-PHENYLPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:**

Prepared by Procedure A and Scheme AN using 4-bromophenol and *N*-(3-[1-(5-hydroxy-5-phenylpentyl)-4-piperidinyl]phenyl)-2-methylpropanamide: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), HCl salt  $\delta$  7.74-6.66 (m, 13H), 5.13-5.02 (m, 1H), 3.73-3.51 (m, br, 2H), 3.05-2.83 (br, 2H), 2.83-2.62 (br, 4H), 2.62-2.42 (m, br, 2H), 2.10-1.80 (m, br, 6H), 1.65-1.37 (m, br, 2H), 1.25 (d, 6H,  $J = 6.8$  Hz); ESMS  $m/e$ : 562.9 ( $M + H$ )<sup>+</sup>.

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#### Example 925

***N*-(3-{1-[5-(4-CHLOROPHENYL)-5-(4-METHOXYPHENOXY)PENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:**

Prepared by Procedure A and Scheme AN using 4-methoxyphenol and *N*-(3-{1-[5-(4-chlorophenyl)-5-hydroxypentyl]-4-piperidinyl}phenyl)-2-methylpropanamide: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), HCl salt  $\delta$  8.13 (s, br, 1H), 7.72-6.70 (m, 12H), 5.08-4.97 (m, 1H), 3.72 (s, 3H), 3.66-3.50 (m, br, 2H), 3.03-2.82 (br, 2H), 2.80-2.54 (m, br, 4H), 2.53-2.17 (m, br, 2H), 2.08-1.78 (m, br, 6H), 1.65-1.38 (m, br, 2H), 1.25 (d, 6H,  $J = 6.8$  Hz). Anal. Calc. for  $C_{33}H_{42}Cl_2N_2O_3 \cdot 0.54CH_2Cl_2$ : C, 63.80; H, 6.88; N, 4.44. Found: C, 63.84; H, 7.18; N, 4.00. ESMS  $m/e$ : 549.1 ( $M + H$ )<sup>+</sup>.

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**Example 926**

**N-(3-{1-[5-(4-FLUOROPHENOXY)-5-(4-FLUOROPHENYL)PENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 4-fluorophenol and N-(3-{1-[5-(4-fluorophenyl)-5-hydroxypentyl]-4-piperidinyl}phenyl)-2-methylpropanamide:  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ), HCl salt  $\delta$  7.62-6.70 (m, 12H), 5.10-5.00 (m, 1H), 3.71-3.56 (m, br, 2H), 3.04-2.82 (br, 2H), 2.78-2.64 (m, br, 3H), 2.64-2.48 (m, br, 3H), 2.05-1.82 (m, br, 6H), 1.62-1.42 (m, br, 2H), 1.25 (d, 6H,  $J = 6.0$  Hz); ESMS  $m/e$ : 521.2 ( $M + H$ ) $^+$ .

**Example 927**

**N-(3-{1-[5-(3-ACETYLPHENOXY)-5-PHENYLPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 1-(3-hydroxyphenyl)ethanone and N-{3-[1-(5-hydroxy-5-phenylpentyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS  $m/e$ : 526.9 ( $M + H$ ) $^+$ .

**Example 928**

**N-(3-{1-[5-(4-METHOXYPHENOXY)-5-PHENYLPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 4-methoxyphenol and N-{3-[1-(5-hydroxy-5-phenylpentyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS  $m/e$ : 515.6 ( $M + H$ ) $^+$ .

**Example 929**

**N-[3-(1-{5-[2-FLUORO-5-(TRIFLUOROMETHYL)PHENOXY]-5-[4-(TRIFLUOROMETHYL)PHENYL]PENTYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 2-fluoro-5-(trifluoromethyl)phenol and N-[3-(1-{5-hydroxy-5-[4-(trifluoromethyl)phenyl]pentyl}-4-

piperidinyl)phenyl]-2-  
 m/e: 639.2 (M + H)<sup>+</sup>.

methylpropanamide: ESMS

### Example 930

5 **N-[3-(1-{5-(3-CHLOROPHENYL)-5-[2-FLUORO-5-(TRIFLUOROMETHYL)PHENOXY]PENTYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 2-fluoro-5-(trifluoromethyl)phenol and N-(3-{1-[5-(3-chlorophenyl)-5-hydroxypentyl]-4-  
 10 piperidinyl}phenyl)-2-methylpropanamide: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), HCl salt δ 8.17 (s, br, 1H), 7.75-6.88 (m, 11H), 5.26-5.14 (m, 1H), 3.68-3.56 (m, br, 2H), 3.05-2.90 (br, 2H), 2.90-2.60 (m, br, 4H), 2.56-2.36 (m, br, 2H), 2.18-1.84 (m, br, 6H), 1.70-1.44 (m, br, 2H), 1.25 (d, 6H, J = 7.2 Hz). Anal. Calc. for C<sub>33</sub>H<sub>38</sub>Cl<sub>2</sub>F<sub>4</sub>N<sub>2</sub>O<sub>2</sub>·0.9EtOAc: C, 60.98; H, 6.32; N, 3.89; Found: C, 60.99; H, 6.17; N, 3.81. ESMS m/e: 605.2 (M + H)<sup>+</sup>.

### Example 931

20 **N-[3-(1-{5-(2-FLUOROPHENYL)-5-[2-FLUORO-5-(TRIFLUOROMETHYL)PHENOXY]PENTYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 2-fluoro-5-(trifluoromethyl)phenol and N-(3-{1-[5-(2-fluorophenyl)-5-hydroxypentyl]-4-  
 25 piperidinyl}phenyl)-2-methylpropanamide: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), HCl salt δ 7.89 (s, br, 1H), 7.72-6.88 (m, 11H), 5.59-5.48 (m, 1H), 3.70-3.48 (br, 2H), 3.05-2.84 (br, 2H), 2.82-2.58 (m, br, 4H), 2.58-2.40 (m, br, 2H), 2.22-1.82 (m, br, 6H), 1.71-1.42 (m, br, 2H), 1.25 (d, 6H, J = 6.4 Hz); ESMS m/e: 589.3 (M + H)<sup>+</sup>.



**Example 932**

**N-[3-(1-{5-(3-FLUOROPHENYL)-5-[2-FLUORO-5-(TRIFLUOROMETHYL)PHENOXY]PENTYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 2-fluoro-5-(trifluoromethyl)phenol and N-(3-{1-[5-(3-fluorophenyl)-5-hydroxypentyl]-4-piperidinyl}phenyl)-2-methylpropanamide:  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ), HCl salt  $\delta$  7.79 (s, br, 1H), 7.63-6.82 (m, 11H), 5.24-5.15 (m, 1H), 3.70-3.56 (br, 2H), 3.04-2.84 (br, 2H), 2.82-2.60 (m, br, 4H), 2.60-2.42 (m, br, 2H), 2.20-1.83 (m, br, 6H), 1.70-1.44 (m, br, 2H), 1.25 (d, 6H,  $J = 6.4$  Hz); ESMS  $m/e$ : 589.3 ( $M + H$ ) $^+$ .

**Example 933**

**N-(3-{1-[5-(3-ACETYLPHENOXY)-5-(4-CHLOROPHENYL)PENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 1-(3-hydroxyphenyl)ethanone and N-(3-{1-[5-(4-chlorophenyl)-5-hydroxypentyl]-4-piperidinyl}phenyl)-2-methylpropanamide:  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ), HCl salt  $\delta$  8.05 (s, br, 1H), 7.74-6.88 (m, 12H), 5.27-5.16 (m, 1H), 3.69-3.52 (m, br, 2H), 3.10-2.81 (br, 2H), 2.81-2.57 (m, br, 4H), 2.54 (s, 3H), 2.52-2.40 (m, br, 2H), 2.05-1.80 (m, br, 6H), 1.66-1.42 (m, br, 2H), 1.25 (d, 6H,  $J = 6.8$  Hz); Anal. Calc. for  $\text{C}_{34}\text{H}_{42}\text{Cl}_2\text{N}_2\text{O}_3 \cdot 0.5\text{CH}_2\text{Cl}_2 \cdot 1.0\text{H}_2\text{O}$ : C, 63.46; H, 6.91; N, 4.30. Found: C, 63.46; H, 7.09; N, 4.00. ESMS  $m/e$ : 561.1 ( $M + H$ ) $^+$ .

**Example 934**

**N-[3-(1-{5-(4-CHLOROPHENYL)-5-[2-FLUORO-5-(TRIFLUOROMETHYL)PHENOXY]PENTYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 2-fluoro-5-(trifluoromethyl)phenol and N-(3-{1-

[5-(4-chlorophenyl)-5-hydroxypentyl]-4-piperidinyl}phenyl)-2-methylpropanamide:  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ), HCl salt  $\delta$  7.61-6.92 (m, 11H), 5.24-5.16 (m, 1H), 3.70-3.58 (m, 2H), 3.02-2.91 (br, 2H), 2.80-2.64 (m, br, 3H), 2.64-2.50 (m, 3H), 2.18-1.94 (m, br, 6H), 1.62-1.44 (m, br, 2H), 1.25 (d, 6H,  $J = 7.2$  Hz); ESMS  $m/e$ : 605.3 ( $M + H$ ) $^+$ .

**Example 935**

10 ***N*-(3-(1-{5-(4-FLUOROPHENYL)-5-[2-FLUORO-5-(TRIFLUOROMETHYL)PHENOXY]PENTYL}-4-PIPERIDINYL)PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 2-fluoro-5-(trifluoromethyl)phenol *N*-(3-{1-[5-(4-fluorophenyl)-5-hydroxypentyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS  $m/e$ : 589.3 ( $M + H$ ) $^+$ .

**Example 936**

20 ***N*-(3-{1-[5-(4-BROMOPHENOXY)-5-(4-CHLOROPHENYL)PENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 4-bromophenol and *N*-(3-{1-[5-(4-chlorophenyl)-5-hydroxypentyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS  $m/e$ : 597.2 ( $M + H$ ) $^+$ .

**Example 937**

25 ***N*-(3-{1-[5-(4-CHLOROPHENOXY)-5-(4-FLUOROPHENYL)PENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 4-chlorophenol and *N*-(3-{1-[5-(4-fluorophenyl)-5-hydroxypentyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS  $m/e$ : 537.3 ( $M + H$ ) $^+$ .

**Example 938**

***N*-(3-{1-[5-(2-ACETYLPHENOXY)-5-PHENYLPENTYL]-4-**

**PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by

Procedure A and Scheme AN using 1-(2-

5 hydroxyphenyl)ethanone and *N*-{3-[1-(5-hydroxy-5-

phenylpentyl)-4-piperidinyl]phenyl}-2-methylpropanamide:

ESMS *m/e*: 527.0 (*M* + *H*)<sup>+</sup>.

**Example 939**

10 ***N*-(3-{1-[5-(2-ETHOXYPHENOXY)-5-PHENYLPENTYL]-4-**

**PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by

Procedure A and Scheme AN using 2-ethoxyphenol and *N*-{3-

[1-(5-hydroxy-5-phenylpentyl)-4-piperidinyl]phenyl}-2-

methylpropanamide: ESMS *m/e*: 529.2 (*M* + *H*)<sup>+</sup>.

15

**Example 940**

***N*-(3-{1-[5-(4-FLUOROPHENOXY)-5-PHENYLPENTYL]-4-**

**PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by

Procedure A and Scheme AN using 4-fluorophenol and *N*-{3-

20 [1-(5-hydroxy-5-phenylpentyl)-4-piperidinyl]phenyl}-2-

methylpropanamide: ESMS *m/e*: 503.2 (*M* + *H*)<sup>+</sup>.

**Example 941**

***N*-(3-{1-[4-(4-FLUOROPHENYL)-4-OXOBUTYL]-4-**

25 **PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by

Procedure K (KI) and Scheme E (K<sub>2</sub>CO<sub>3</sub>) using 2-methyl-*N*-

[3-(4-piperidinyl)phenyl]propanamide and 4-chloro-1-(4-

fluorophenyl)-1-butanone: ESMS *m/e*: 411.2 (*M* + *H*)<sup>+</sup>.

30

**Example 942**

**2-METHYL-*N*-(3-{1-[3-(1H-PYRROL-3-YL) PROPYL]-4-**

**PIPERIDINYL}PHENYL) PROPANAMIDE:** Prepared by Procedure K

(KI) and Scheme E (K<sub>2</sub>CO<sub>3</sub>) using 2-methyl-*N*-[3-(4-

piperidinyl)phenyl]propanamide and 3-(3-bromopropyl)-1H-pyrrole: ESMS  $m/e$ : 354.2 ( $M + H$ )<sup>+</sup>.

#### Example 943

5 ***N*-(3-{1-[4-(4-ISOPROPYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure K (KI) and Scheme E ( $K_2CO_3$ ) using 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide and 4-chloro-1-(4-isopropylphenyl)-1-butanone: ESMS  $m/e$ : 435.2 ( $M + H$ )<sup>+</sup>.

10

#### Example 944

***N*-(3-{1-[4-(4-METHOXYPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure K (KI) and Scheme E ( $K_2CO_3$ ) using 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide and 4-chloro-1-(4-methoxyphenyl)-1-butanone: ESMS  $m/e$ : 423.2 ( $M + H$ )<sup>+</sup>.

15

#### Example 945

**2-METHYL-*N*-(3-{1-[4-(4-METHYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE:** Prepared by Procedure K (KI) and Scheme E ( $K_2CO_3$ ) using 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide and 4-chloro-1-(4-methylphenyl)-1-butanone: ESMS  $m/e$ : 407.2 ( $M + H$ )<sup>+</sup>.

20

#### Example 946

***N*-(3-{1-[4-(4-TERT-BUTYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure K (KI) and Scheme E ( $K_2CO_3$ ) using 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide and 1-(4-tert-butylphenyl)-4-chloro-1-butanone: ESMS  $m/e$ : 449.2 ( $M + H$ )<sup>+</sup>.

25

30

#### Example 947

***N*-(3-{1-[4-(4-BROMOPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure K (KI) and Scheme E (K<sub>2</sub>CO<sub>3</sub>) using 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide and 1-(4-bromophenyl)-4-chloro-1-butanone: ESMS *m/e*: 471.3 (M + H)<sup>+</sup>.

**Example 948**

**2-METHYL-*N*-(3-{1-[4-OXO-4-(2-THIENYL)BUTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE:** Prepared by Procedure K (KI) and Scheme E (K<sub>2</sub>CO<sub>3</sub>) using 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide and 4-chloro-1-(2-thienyl)-1-butanone: ESMS *m/e*: 399.1 (M + H)<sup>+</sup>.

## II. Synthetic Methods for General Structures

The examples described in Section I are merely illustrative of the methods used to synthesize MCH1 antagonists. Further derivatives may be obtained  
5 utilizing generalized methods based on the synthetic methods used to synthesize the examples.

It may be necessary to incorporate protection and deprotection strategies for substituents such as amino,  
10 amido, carboxylic acid, and hydroxyl groups in the generalized synthetic methods to form further derivatives. Methods for protection and deprotection of such groups are well-known in the art, and may be found, for example in Green, T.W. and Wuts, P.G.M. (1991)  
15 Protection Groups in Organic Synthesis, 2<sup>nd</sup> Edition John Wiley & Sons, New York.

## III. Oral Compositions

As a specific embodiment of an oral composition of a  
20 compound of this invention, 100 mg of one of the compounds described herein is formulated with sufficient finely divided lactose to provide a total amount of 580 to 590 mg to fill a size O hard gel capsule.

## 25 IV. Pharmacological Evaluation of Compounds at Cloned rat MCH1 Receptor

The pharmacological properties of the compounds of the present invention were evaluated at the cloned rat MCH1 receptor using protocols described below.

30

### Host Cells

A broad variety of host cells can be used to study heterologously expressed proteins. These cells include but are not restricted to assorted mammalian lines such as: Cos-7, CHO, LM(tk-), HEK293, Peak rapid 293, etc.;  
5 insect cell lines such as: Sf9, Sf21, etc.; amphibian cells such as xenopus oocytes; and others.

COS 7 cells are grown on 150 mm plates in DMEM with supplements (Dulbecco's Modified Eagle Medium with 10%  
10 bovine calf serum, 4 mM glutamine, 100 units/ml penicillin/100 Fg/ml streptomycin) at 37°C, 5% CO<sub>2</sub>. Stock plates of COS-7 cells are trypsinized and split 1:6 every 3-4 days.

15 Human embryonic kidney 293 cells are grown on 150 mm plates in DMEM with supplements (10% bovine calf serum, 4 mM glutamine, 100 units/ml penicillin/100 Fg/ml streptomycin) at 37°C, 5% CO<sub>2</sub>. Stock plates of 293 cells are trypsinized and split 1:6 every 3-4 days.

20 Human embryonic kidney Peak rapid 293 (Peakr293) cells are grown on 150 mm plates in DMEM with supplements (10% fetal bovine serum, 10% L-glutamine, 50 Fg/ml gentamycin) at 37°C, 5% CO<sub>2</sub>. Stock plates of Peak rapid  
25 293 cells are trypsinized and split 1:12 every 3-4 days.

Mouse fibroblast LM(tk-) cells are grown on 150 mm plates in DMEM with supplements (Dulbecco's Modified Eagle Medium with 10% bovine calf serum, 4 mM glutamine,  
30 100 units/ml penicillin/100 Fg/ml streptomycin) at 37°C, 5% CO<sub>2</sub>. Stock plates of LM(tk-) cells are trypsinized and split 1:10 every 3-4 days.

Chinese hamster ovary (CHO) cells were grown on 150 mm plates in HAM's F-12 medium with supplements (10% bovine calf serum, 4 mM L-glutamine and 100 units/ml penicillin/ 100 Fg/ml streptomycin) at 37°C, 5% CO<sub>2</sub>.  
5 Stock plates of CHO cells are trypsinized and split 1:8 every 3-4 days.

Mouse embryonic fibroblast NIH-3T3 cells are grown on 150 mm plates in Dulbecco's Modified Eagle Medium (DMEM)  
10 with supplements (10% bovine calf serum, 4 mM glutamine, 100 units/ml penicillin/100 Fg/ml streptomycin) at 37°C, 5% CO<sub>2</sub>. Stock plates of NIH-3T3 cells are trypsinized and split 1:15 every 3-4 days.

15 Sf9 and Sf21 cells are grown in monolayers on 150 mm tissue culture dishes in TMN-FH media supplemented with 10% fetal calf serum, at 27°C, no CO<sub>2</sub>. High Five insect cells are grown on 150 mm tissue culture dishes in Ex-Cell 400™ medium supplemented with L-Glutamine, also at  
20 27°C, no CO<sub>2</sub>.

In some cases, cell lines that grow as adherent monolayers can be converted to suspension culture to increase cell yield and provide large batches of uniform  
25 assay material for routine receptor screening projects.

#### Transient expression

DNA encoding proteins to be studied can be transiently expressed in a variety of mammalian, insect, amphibian  
30 and other cell lines by several methods including but not restricted to; calcium phosphate-mediated, DEAE-dextran mediated, Liposomal-mediated, viral-mediated, electroporation-mediated and microinjection delivery.



Each of these methods may require optimization of assorted experimental parameters depending on the DNA, cell line, and the type of assay to be subsequently employed.

5

A typical protocol for the calcium phosphate method as applied to Peak rapid 293 cells is described as follows:

10

Adherent cells are harvested approximately twenty-four hours before transfection and replated at a density of  $3.5 \times 10^6$  cells/dish in a 150 mm tissue culture dish and allowed to incubate over night at 37°C at 5% CO<sub>2</sub>. 250 Fl of a mixture of CaCl<sub>2</sub> and DNA (15 Fg DNA in 250 mM CaCl<sub>2</sub>) is added to a 5 ml plastic tube and 500 Fl of 2X HBS (280 mM NaCl, 10 mM KCl, 1.5 mM Na<sub>2</sub>HPO<sub>4</sub>, 12 mM dextrose, 50 mM HEPES) is slowly added with gentle mixing. The mixture is allowed to incubate for 20 minutes at room temperature to allow a DNA precipitate to form. The DNA precipitate mixture is then added to the culture medium in each plate and incubated for 5 hours at 37°C, 5% CO<sub>2</sub>. After the incubation, 5ml of culture medium (DMEM, 10% FBS, 10% L-glut and 50 µg/ml gentamycin) is added to each plate. The cells are then incubated for 24 to 48 hours at 37°C, 5% CO<sub>2</sub>.

15

20

25

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A typical protocol for the DEAE-dextran method as applied to Cos-7 cells is described as follows; Cells to be used for transfection are split 24 hours prior to the transfection to provide flasks which are 70-80% confluent at the time of transfection. Briefly, 8 Fg of receptor DNA plus 8 Fg of any additional DNA needed (e.g. G<sub>α</sub> protein expression vector, reporter construct, antibiotic resistance marker, mock vector, etc.) are

added to 9 ml of complete DMEM plus DEAE-dextran mixture (10 mg/ml in PBS). Cos-7 cells plated into a T225 flask (sub-confluent) are washed once with PBS and the DNA mixture is added to each flask. The cells are  
5 allowed to incubate for 30 minutes at 37°C, 5% CO<sub>2</sub>. Following the incubation, 36 ml of complete DMEM with 80 FM chloroquine is added to each flask and allowed to incubate an additional 3 hours. The medium is then aspirated and 24 ml of complete medium containing 10%  
10 DMSO for exactly 2 minutes and then aspirated. The cells are then washed 2 times with PBS and 30 ml of complete DMEM added to each flask. The cells are then allowed to incubate over night. The next day the cells are harvested by trypsinization and reseeded as needed  
15 depending upon the type of assay to be performed.

A typical protocol for liposomal-mediated transfection as applied to CHO cells is described as follows; Cells to be used for transfection are split 24 hours prior to  
20 the transfection to provide flasks which are 70-80% confluent at the time of transfection. A total of 10Fg of DNA which may include varying ratios of receptor DNA plus any additional DNA needed (e.g. G<sub>o</sub> protein expression vector, reporter construct, antibiotic  
resistance marker, mock vector, etc.) is used to  
25 transfect each 75 cm<sup>2</sup> flask of cells. Liposomal mediated transfection is carried out according to the manufacturer=s recommendations (LipofectAMINE, GibcoBRL, Bethesda, MD). Transfected cells are harvested 24 hours  
30 post transfection and used or reseeded according the requirements of the assay to be employed.

A typical protocol for the electroporation method as applied to Cos-7 cells is described as follows; Cells to be used for transfection are split 24 hours prior to the transfection to provide flasks which are subconfluent at the time of transfection. The cells are harvested by trypsinization resuspended in their growth media and counted. 4 x 10<sup>6</sup> cells are suspended in 300 Fl of DMEM and placed into an electroporation cuvette. 8 Fg of receptor DNA plus 8 Fg of any additional DNA needed (e.g. G<sub>a</sub> protein expression vector, reporter construct, antibiotic resistance marker, mock vector, etc.) is added to the cell suspension, the cuvette is placed into a BioRad Gene Pulser and subjected to an electrical pulse (Gene Pulser settings: 0.25 kV voltage, 950 FF capacitance). Following the pulse, 800 Fl of complete DMEM is added to each cuvette and the suspension transferred to a sterile tube. Complete medium is added to each tube to bring the final cell concentration to 1 x 10<sup>5</sup> cells/100 Fl. The cells are then plated as needed depending upon the type of assay to be performed.

A typical protocol for viral mediated expression of heterologous proteins is described as follows for baculovirus infection of insect Sf9 cells. The coding region of DNA encoding the receptor disclosed herein may be subcloned into pBlueBacIII into existing restriction sites or sites engineered into sequences 5' and 3' to the coding region of the polypeptides. To generate baculovirus, 0.5 Fg of viral DNA (BaculoGold) and 3 Fg of DNA construct encoding a polypeptide may be co-transfected into 2 x 10<sup>6</sup> *Spodoptera frugiperda* insect Sf9 cells by the calcium phosphate co-precipitation method, as outlined in by Pharmingen (in "Baculovirus Expression

Vector System: Procedures and Methods Manual"). The cells then are incubated for 5 days at 27°C. The supernatant of the co-transfection plate may be collected by centrifugation and the recombinant virus plaque purified. The procedure to infect cells with virus, to prepare stocks of virus and to titer the virus stocks are as described in Pharmingen's manual. Similar principals would in general apply to mammalian cell expression via retro-viruses, Simliki forest virus and double stranded DNA viruses such as adeno-, herpes-, and vacinia-viruses, and the like.

#### Stable expression

Heterologous DNA can be stably incorporated into host cells, causing the cell to perpetually express a foreign protein. Methods for the delivery of the DNA into the cell are similar to those described above for transient expression but require the co-transfection of an ancillary gene to confer drug resistance on the targeted host cell. The ensuing drug resistance can be exploited to select and maintain cells that have taken up the heterologous DNA. An assortment of resistance genes are available including but not restricted to Neomycin, Kanamycin, and Hygromycin. For the purposes of receptor studies, stable expression of a heterologous receptor protein is carried out in, but not necessarily restricted to, mammalian cells including, CHO, HEK293, LM(tk-), etc.

#### Cell membrane preparation

For binding assays, pellets of transfected cells are suspended in ice-cold buffer (20 mM Tris.HCl, 5 mM EDTA, pH 7.4) and homogenized by sonication for 7 sec. The

cell lysates are centrifuged at 200 x g for 5 min at 4°C. The supernatants are then centrifuged at 40,000 x g for 20 min at 4°C. The resulting pellets are washed once in the homogenization buffer and suspended in binding buffer (see methods for radioligand binding). Protein concentrations are determined by the method of Bradford (1976) using bovine serum albumin as the standard. Binding assays are usually performed immediately, however it is possible to prepare membranes in batch and store frozen in liquid nitrogen for future use.

#### Radioligand binding assays

Radioligand binding assays for the rat MCH1 receptor were carried out using plasmid pcDNA3.1-rMCH1-f (ATCC Patent Deposit Designation No. PTA-3505). Plasmid pcDNA3.1-rMCH1-f comprises the regulatory elements necessary for expression of DNA in a mammalian cell operatively linked to DNA encoding the rat MCH1 receptor so as to permit expression thereof. Plasmid pcDNA3.1-rMCH1-f was deposited on July 05, 2001, with the American Type Culture Collection (ATCC), 12301 Parklawn Drive, Rockville, Maryland 20852, U.S.A. under the provisions of the Budapest Treaty for the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure and was accorded ATCC Patent Deposit Designation No. PTA-3505.

Binding assays can also be performed as described hereinafter using plasmid pEXJ.HR-TL231 (ATCC Accession No. 203197) Plasmid pEXJ.HR-TL231 encodes the human MCH1 receptor and was deposited on September 17, 1998, with the American Type Culture Collection (ATCC), 12301

Parklawn Drive, Rockville, Maryland 20852, U.S.A.  
under the provisions of the Budapest Treaty for the  
International Recognition of the Deposit of  
Microorganisms for the Purposes of Patent Procedure and  
was accorded ATCC Accession No. 203197.

Human embryonic kidney Peak rapid 293 cells (Peakr293  
cells) were transiently transfected with DNA encoding the  
MCH1 receptor utilizing the calcium phosphate method and  
cell membranes were prepared as described above. Binding  
experiments with membranes from Peakr293 cells  
transfected with the rat MCH1 receptor were performed  
with 0.08 nM [<sup>3</sup>H]Compound A (the synthesis of Compound A  
is described in detail below) using an incubation buffer  
consisting of 50 mM Tris pH 7.4, 10 mM MgCl<sub>2</sub>, 0.16 mM  
PMSF, 1 mM 1,10 phenantroline and 0.2% BSA. Binding was  
performed at 25°C for 90 minutes. Incubations were  
terminated by rapid vacuum filtration over GF/C glass  
fiber filters, presoaked in 5% PEI using 50 mM Tris pH  
7.4 as wash buffer. In all experiments, nonspecific  
binding is defined using 10 pM Compound A.

#### Functional assays

Cells may be screened for the presence of endogenous  
mammalian receptor using functional assays. Cells with  
no or a low level of endogenous receptor present may be  
transfected with the exogenous receptor for use in  
functional assays.

30

A wide spectrum of assays can be employed to screen for  
receptor activation. These range from traditional  
measurements of phosphatidyl inositol, cAMP, Ca<sup>++</sup>, and

K<sup>+</sup>, for example; to systems measuring these same second messengers but which have been modified or adapted to be higher throughput, more generic, and more sensitive; to cell based platforms reporting more general cellular events resulting from receptor activation such as metabolic changes, differentiation, and cell division/proliferation, for example; to high level organism assays which monitor complex physiological or behavioral changes thought to be involved with receptor activation including cardiovascular, analgesic, orexigenic, anxiolytic, and sedation effects, for example.

#### Radioligand Binding Assay Results

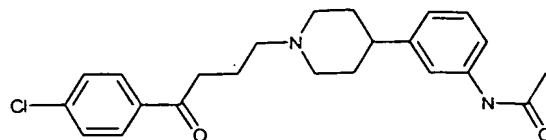
The compounds described above were assayed using cloned rat MCH1. The binding affinities of the compounds are shown in Table I.

EXAMPLE No.	STRUCTURE	Ki (nM) rMCH1
1		90
2		3.9
3		768
4		357
5		14.2
6		274
7		1000
8		627



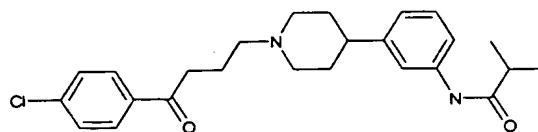
503

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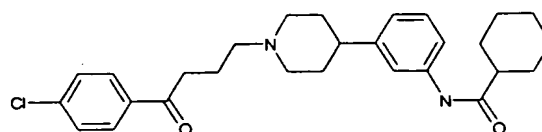
69

10



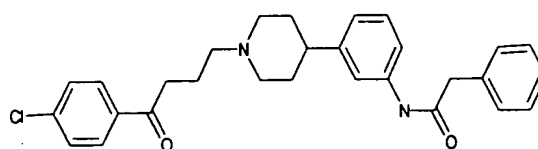
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11



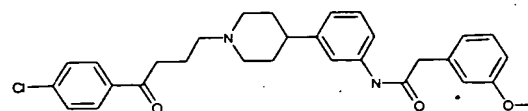
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12



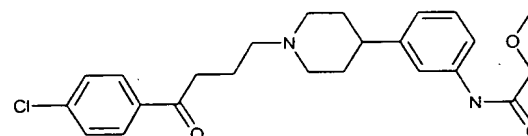
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13



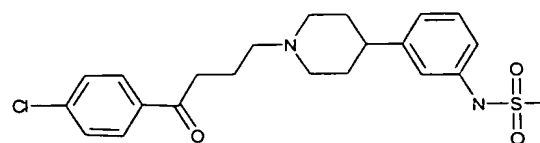
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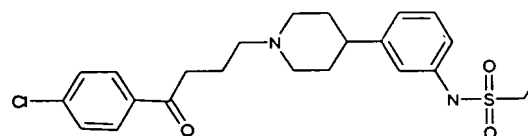
167

15



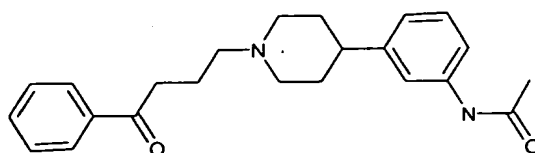
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16



272

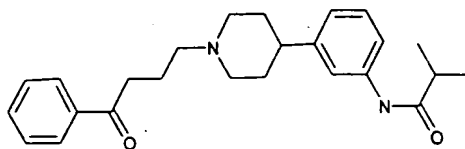
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342

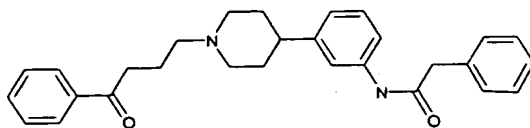
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18



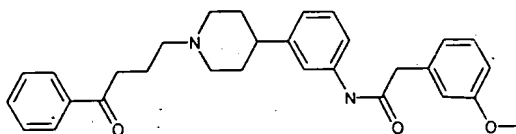
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19



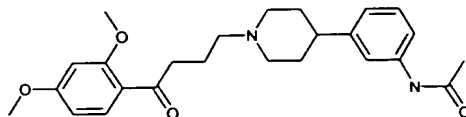
506

20



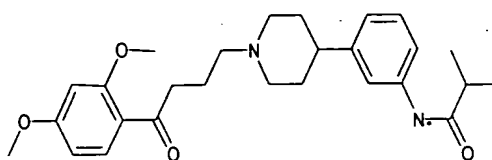
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21



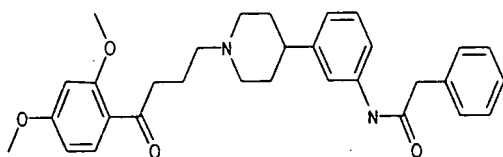
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22



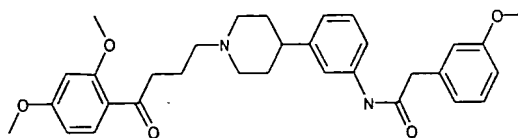
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23



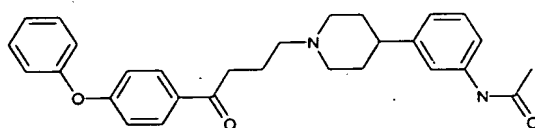
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24



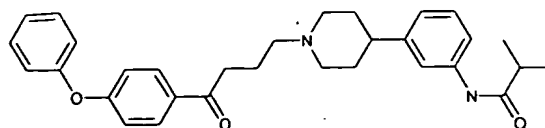
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25

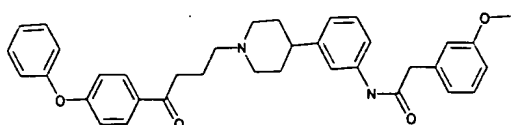
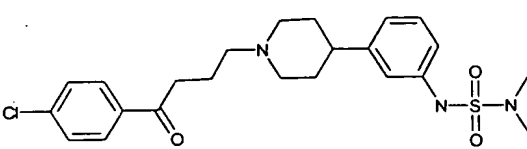
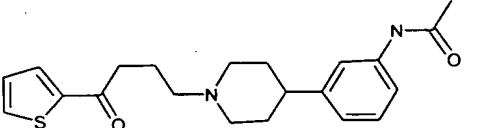
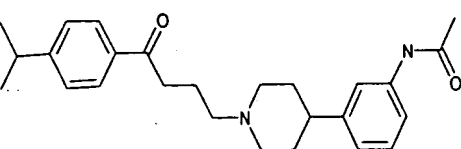
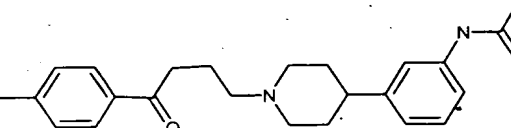
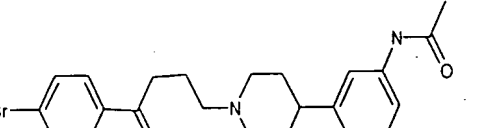
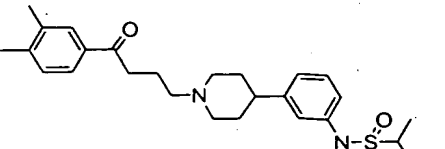
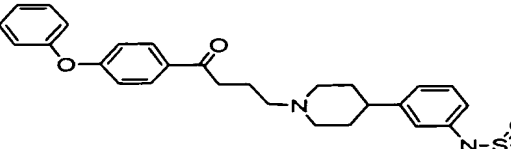
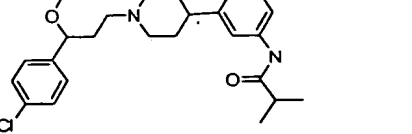


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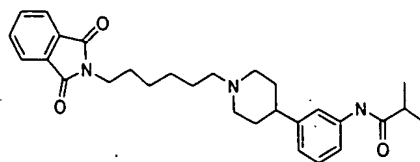
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192

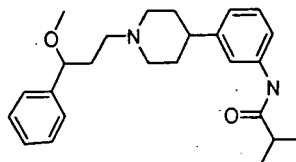
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31		362
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33		615
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35		11.5

36



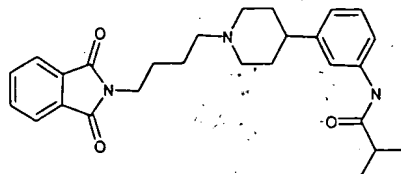
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37



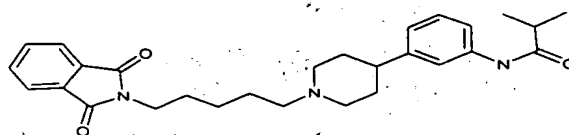
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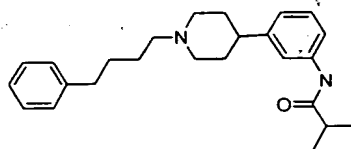
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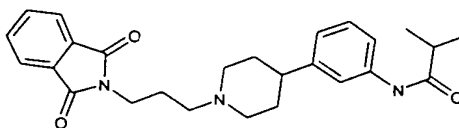
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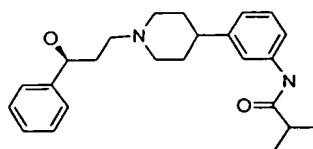
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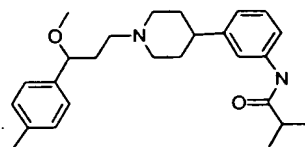
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42



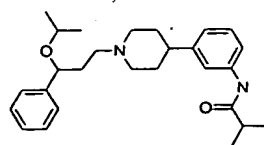
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43



12

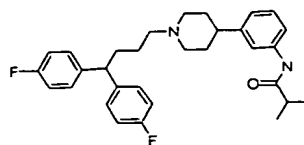
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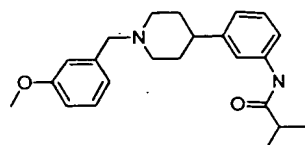
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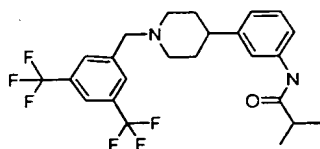
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46



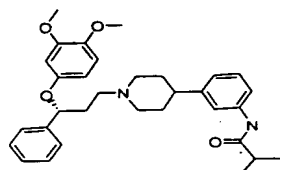
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47



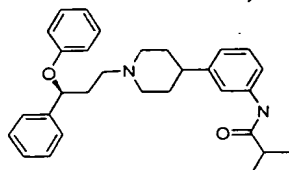
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48



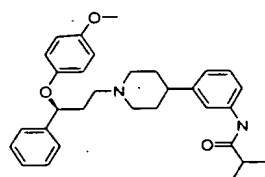
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49



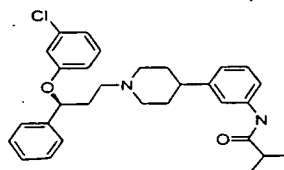
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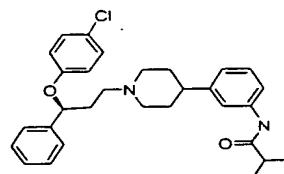
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51



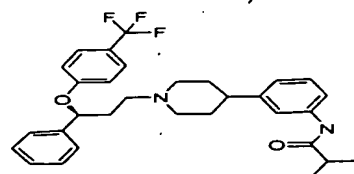
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3.8

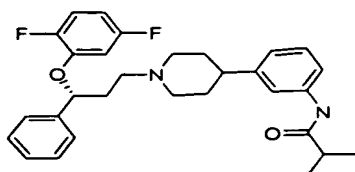
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7.1

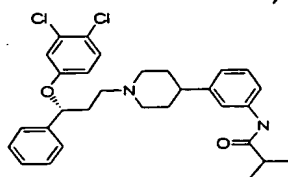
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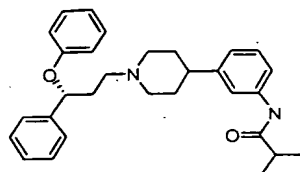
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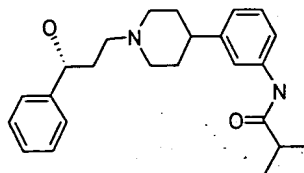
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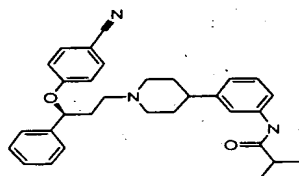
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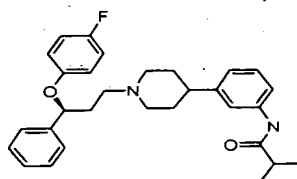
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58



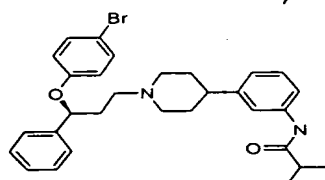
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59



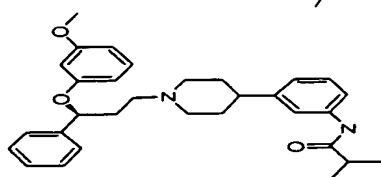
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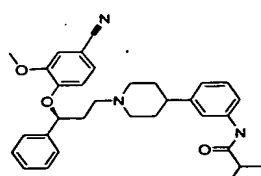
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61

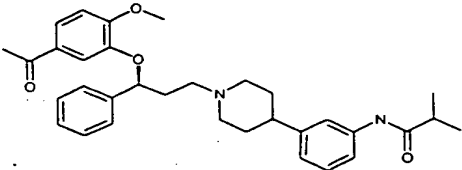
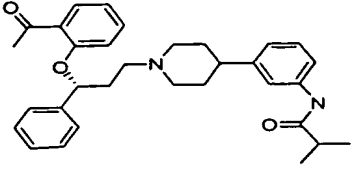
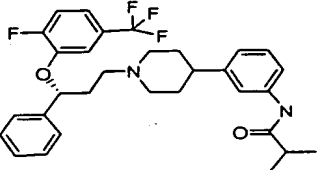
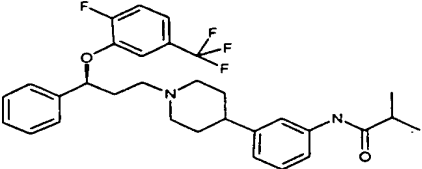
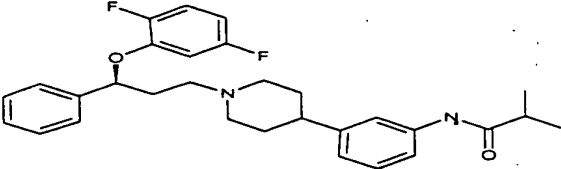
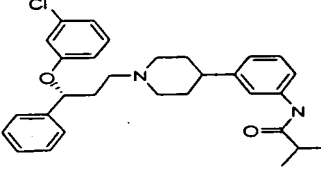
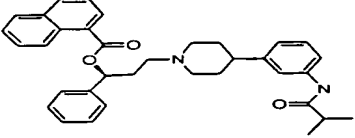
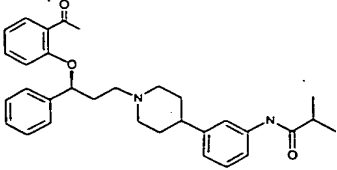


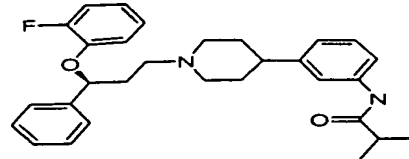
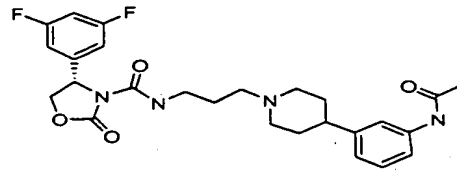
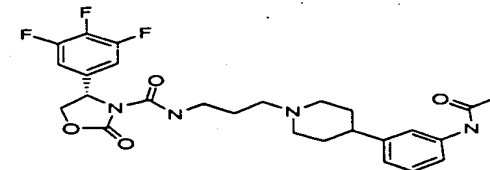
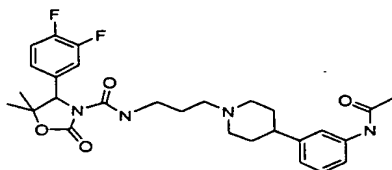
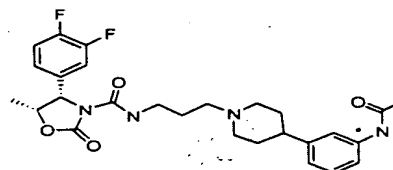
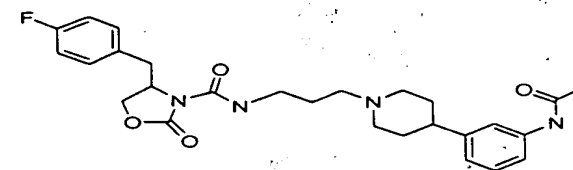
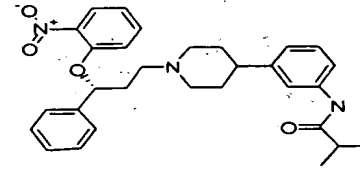
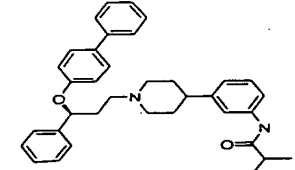
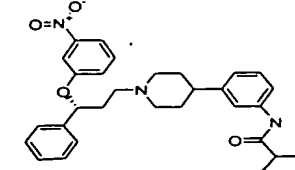
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62



12.8

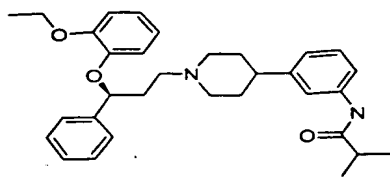
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65		17
66		3.3
67		5.9
68		9.3
69		32.5
70		50

71		6.6
72		31.4
73		22.3
74		48.6
75		11.8
76		44.6
77		25.7
78		22.2
79		19.4



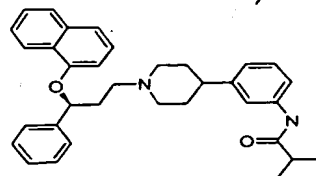
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80



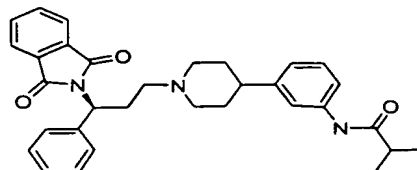
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81



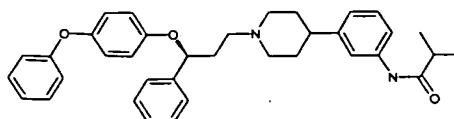
377

82



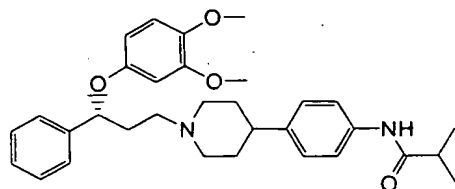
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83



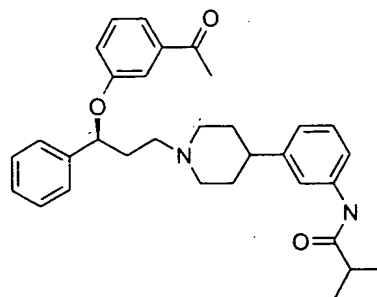
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84



121

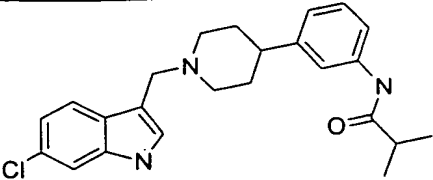
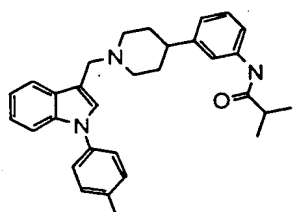
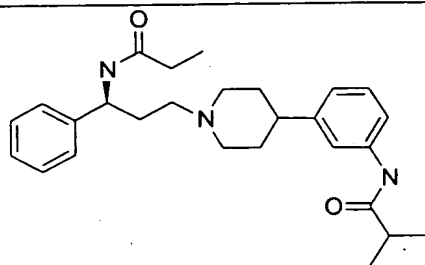
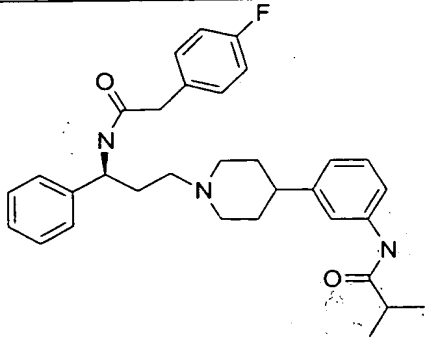
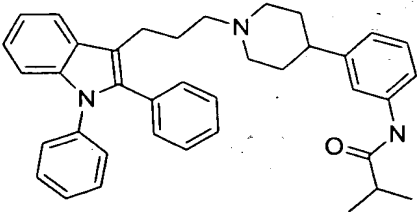
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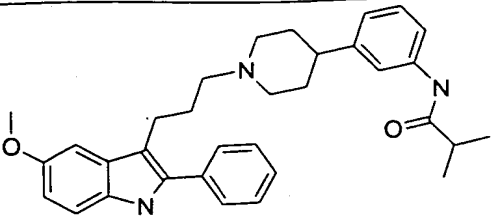
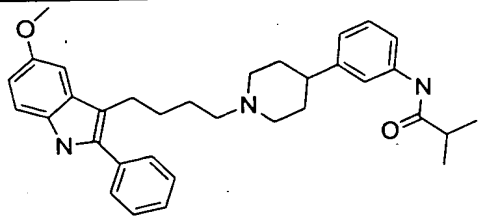
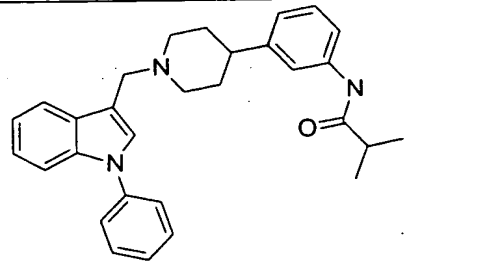
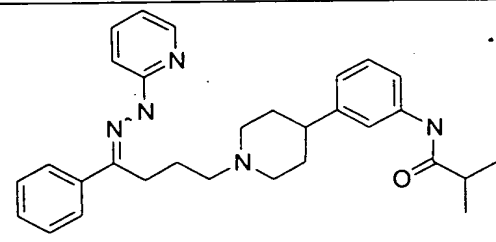
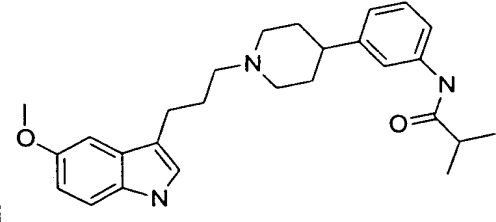
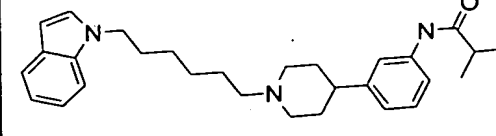


3.2

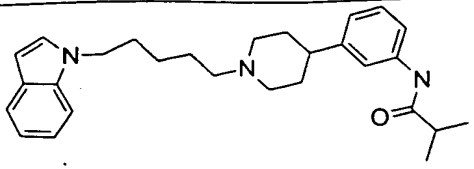
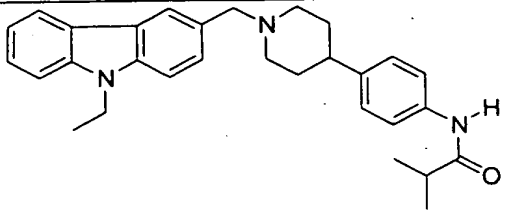
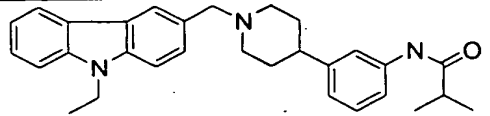
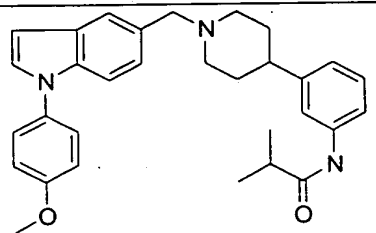
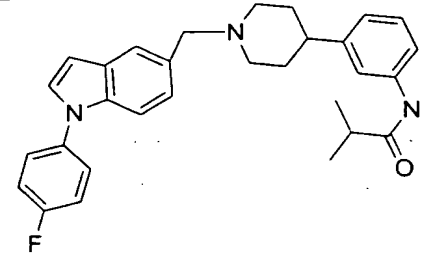
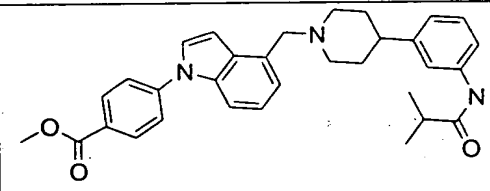
EXAMPLE	STRUCTURE	Ki (nM) rMCH1
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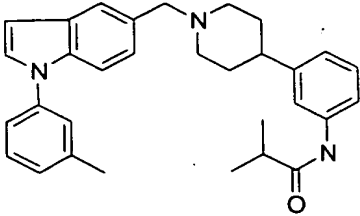
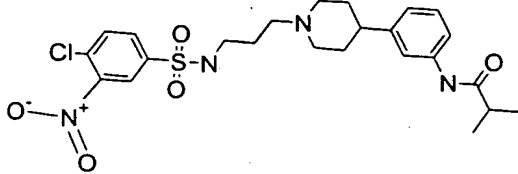
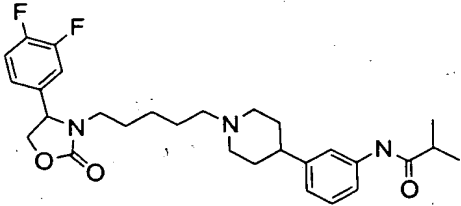
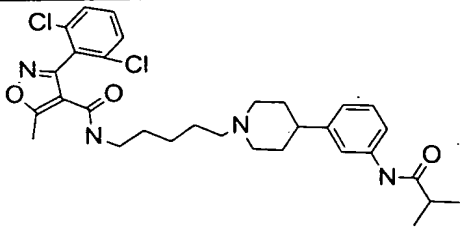
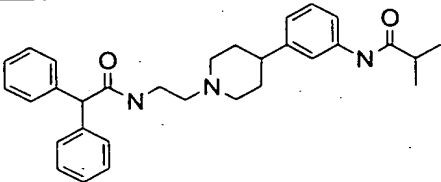
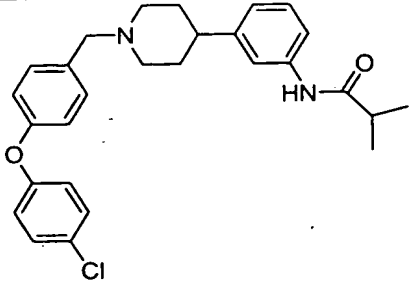
512

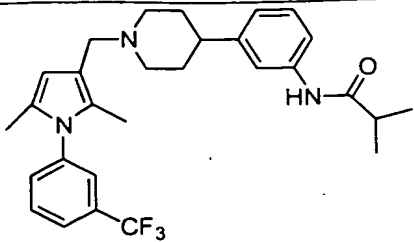
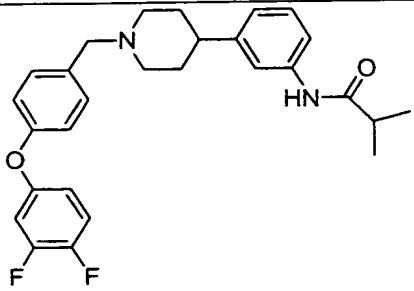
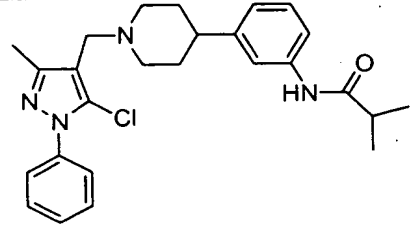
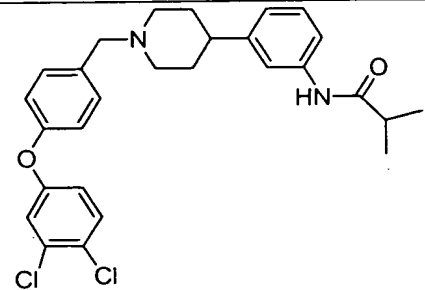
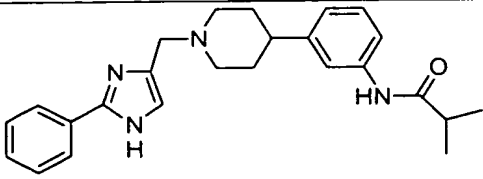
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87		14.9
88		16.0
89		3.0
90		3.0

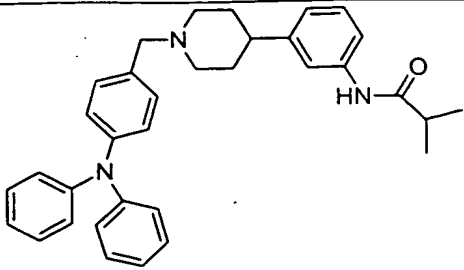
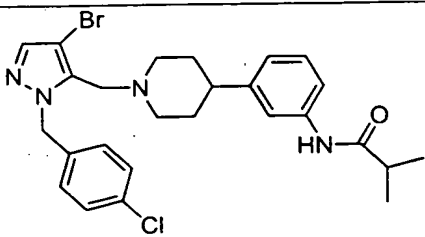
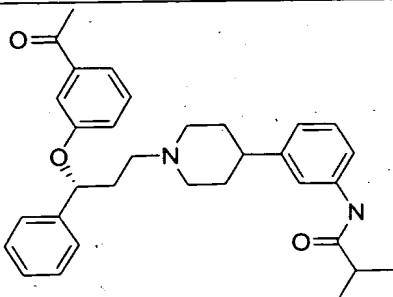
91		2.3
92		8.0
93		4.2
94		2.3
95		5.4
96		15.9

514

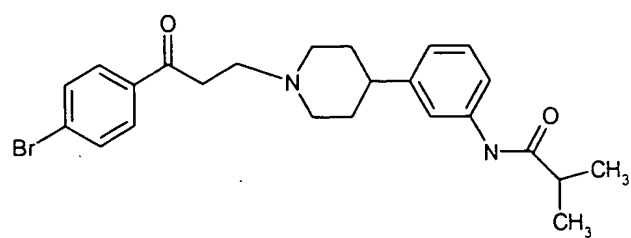
97		27.3
98		37.9
99		1.7
100		27.5
101		7.8
102		38.4

103		21.3
104		11.2
105		4.6
106		7.1
107		1.7
108		5.2

109		20.9
110		1.8
111		ND
112		6.1
113		ND

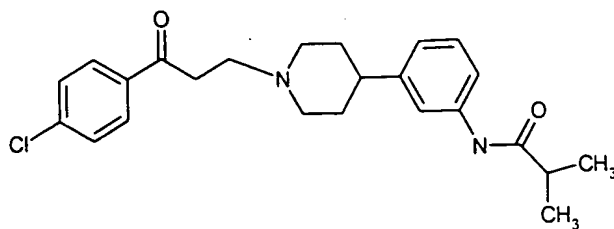
114	<div>517</div> 	3.6
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116		3.8

117

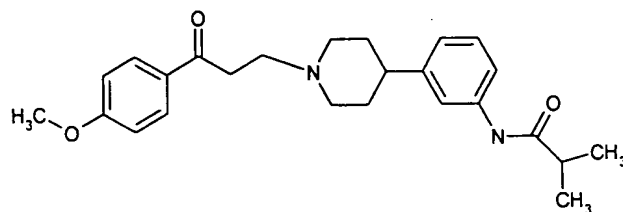


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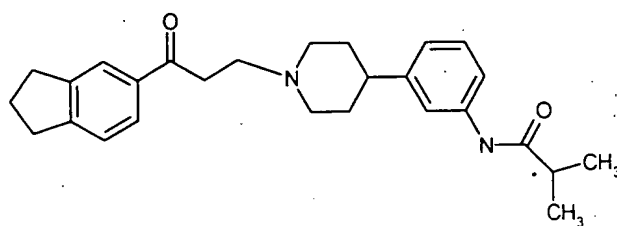
118 518 43.6



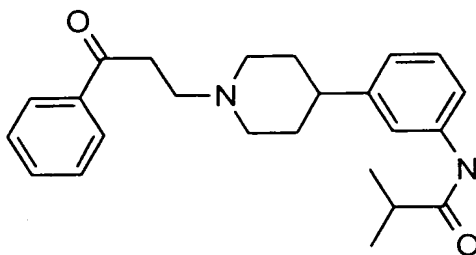
119 75.7



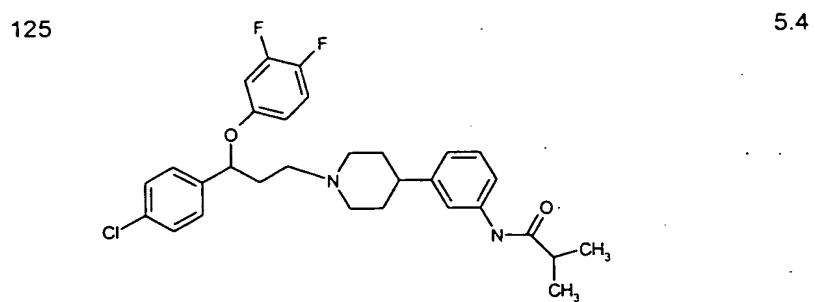
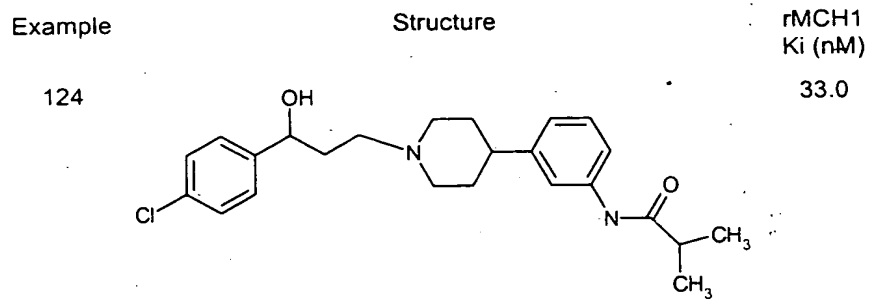
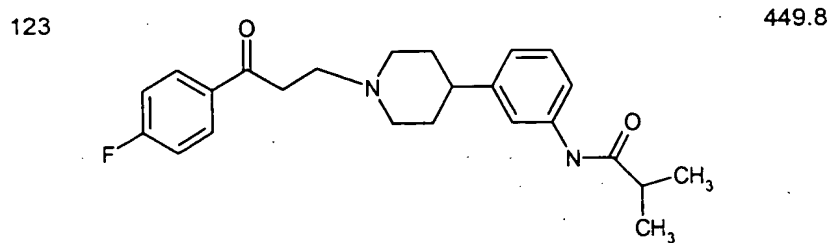
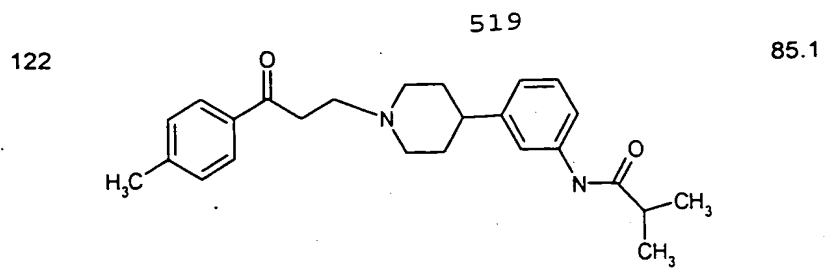
120 31.1



121 183.7

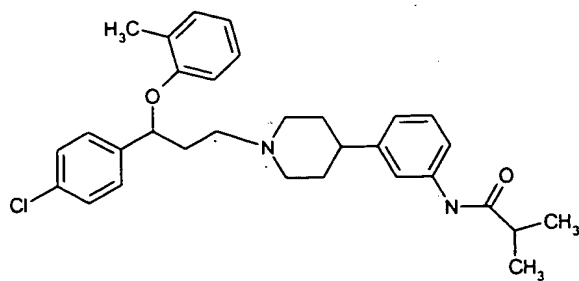






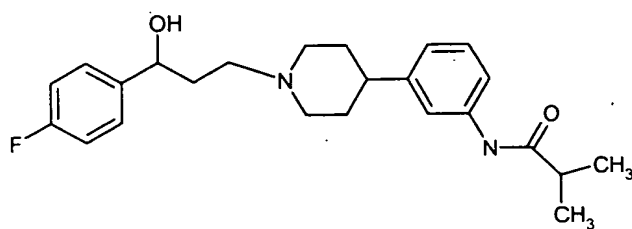
126

13.8



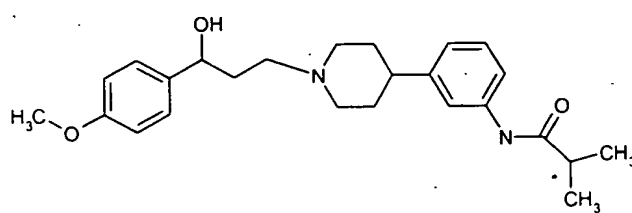
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168.5



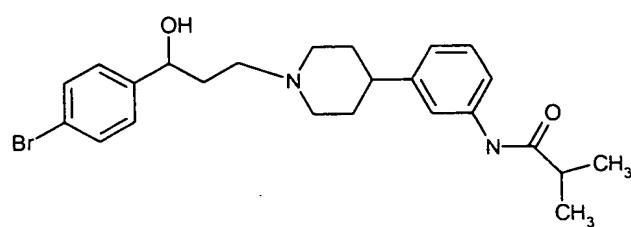
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328.8

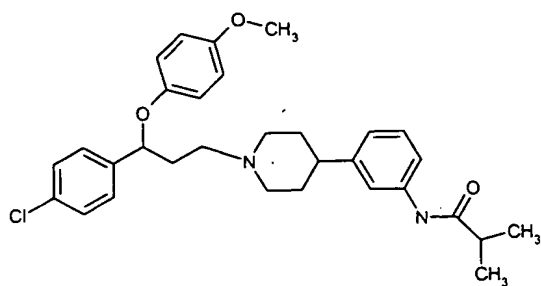


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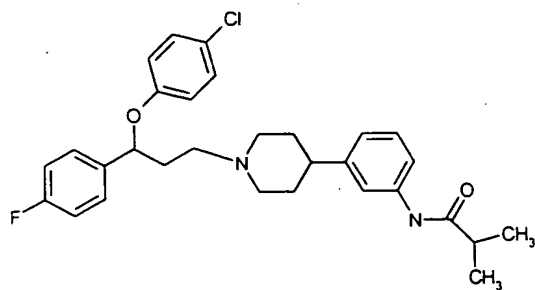
38.8



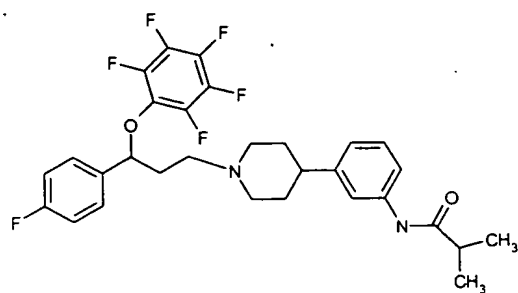
130 521 6.0



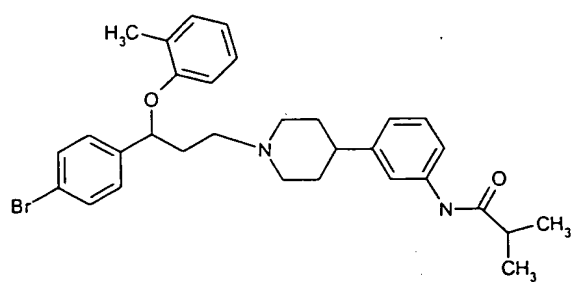
131 11.9



132 41.7

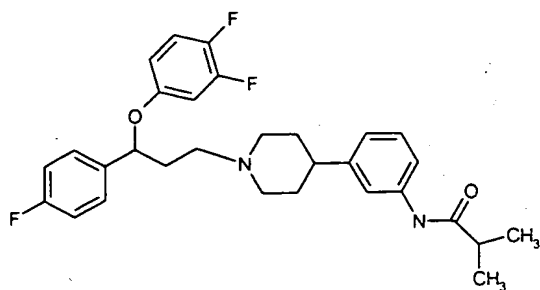


133 14.1



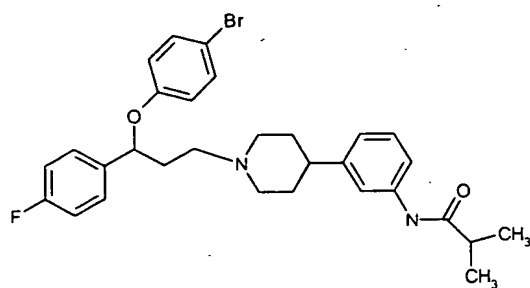
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36.6



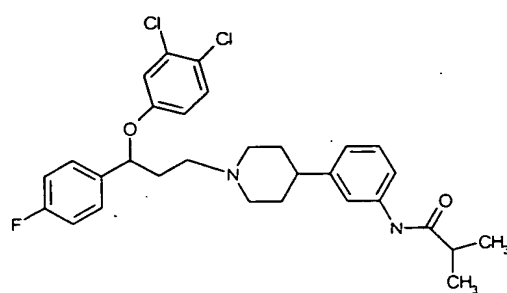
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10.9



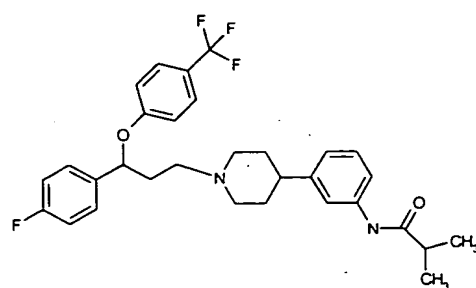
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15.9



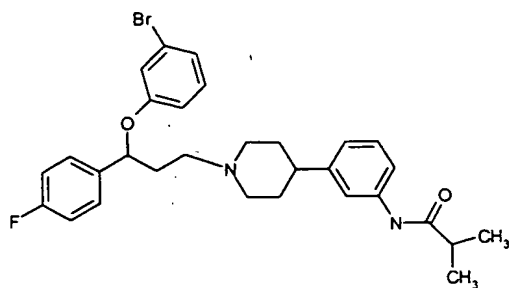
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25.2



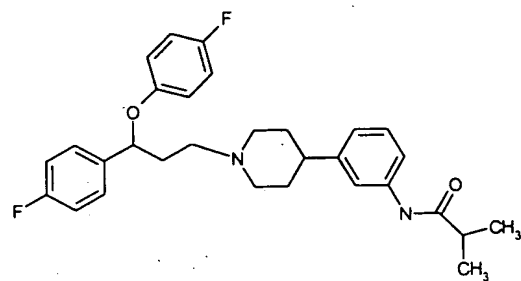
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9.3



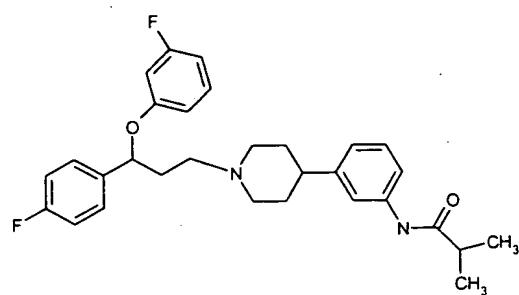
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38.7



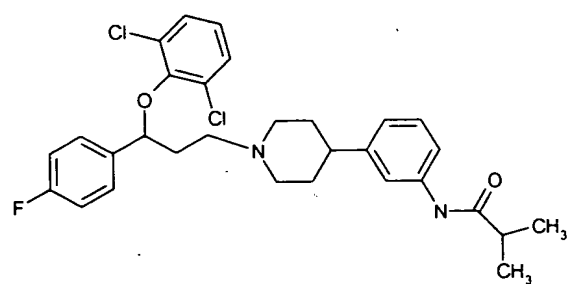
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27.4



141

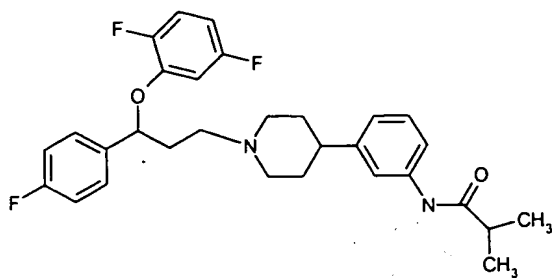
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524

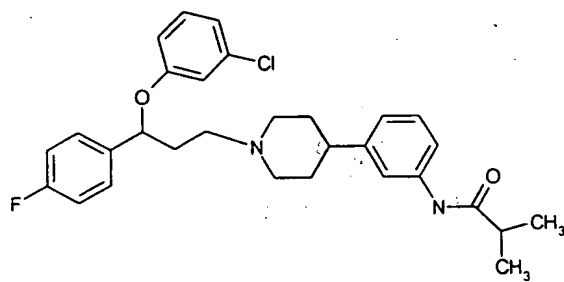
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18.3



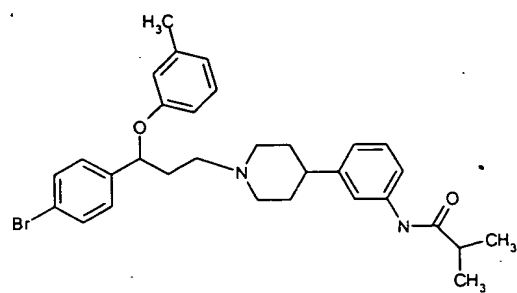
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8.7



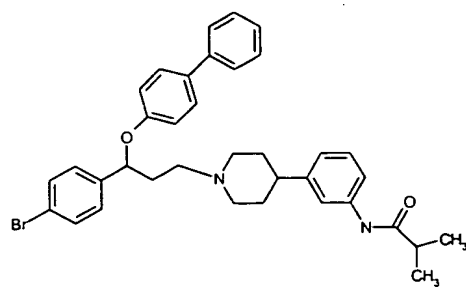
144

13.4



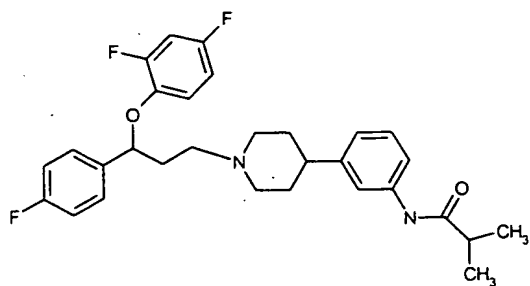
145

196.8



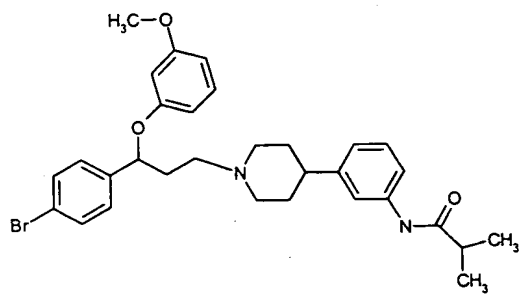
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19.2



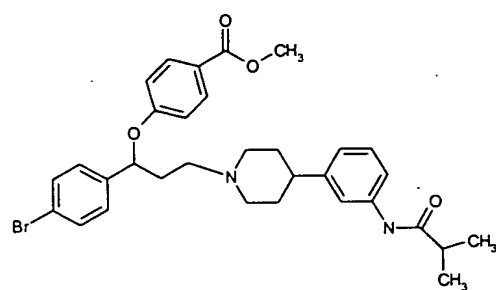
147

8.7



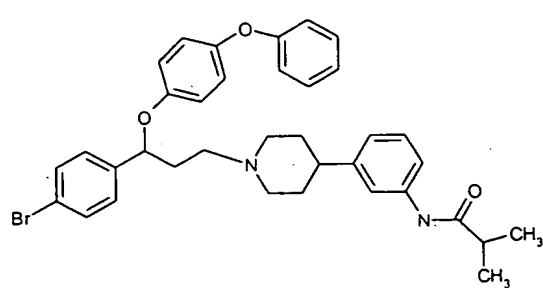
148

24.7



149

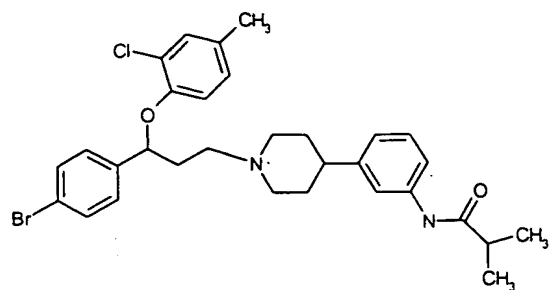
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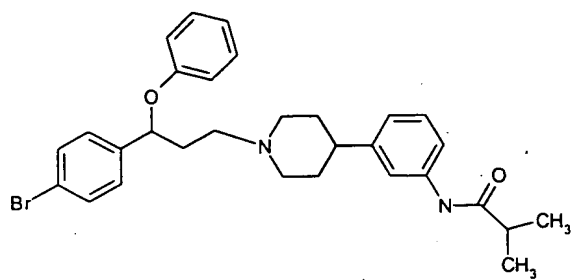
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8.0



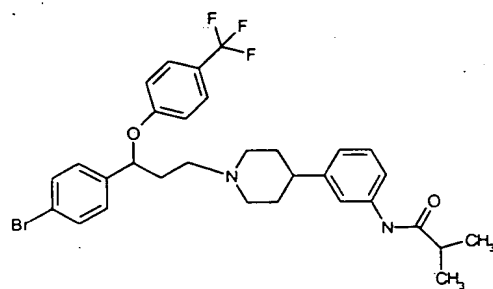
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14.2



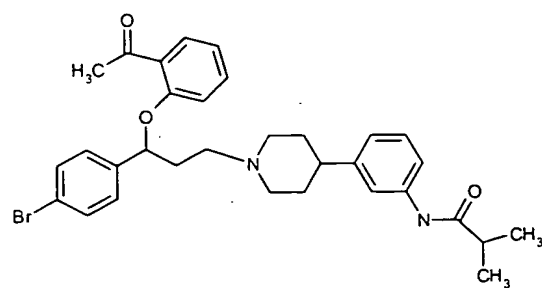
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13.3



153

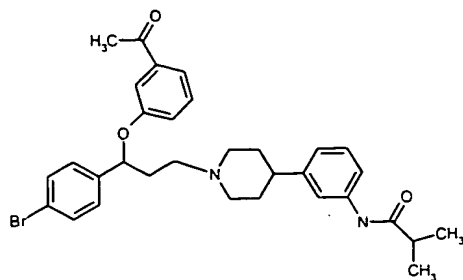
8.1





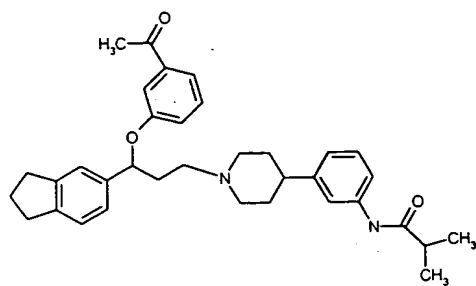
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9.3



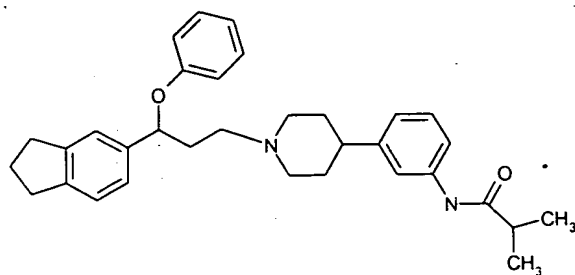
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7.4



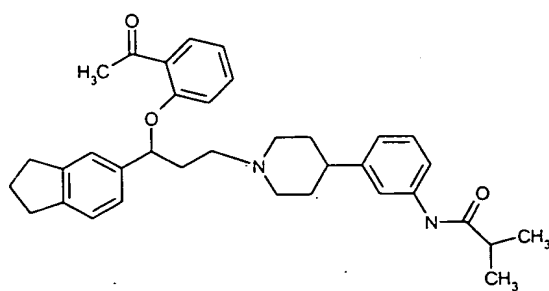
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8.8



157

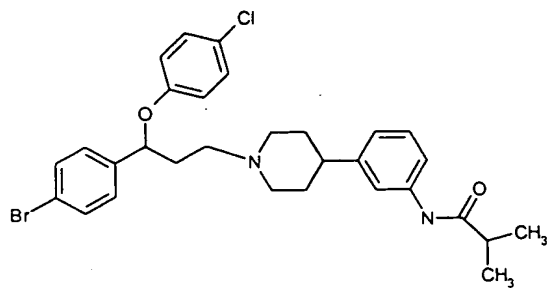
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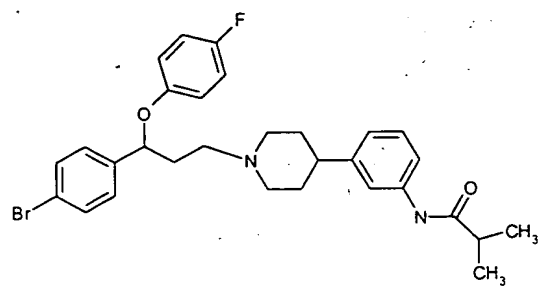
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CC(C)C(=O)Nc1ccc(cc1)C2CCN(CC2)CCOC(=O)c3ccc(Br)cc3

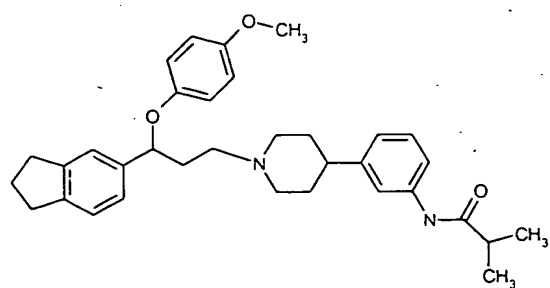
## 4.5



## 6.2

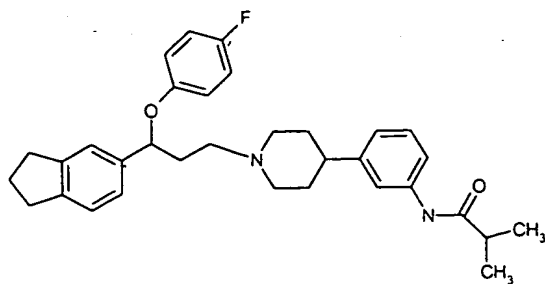


7.9



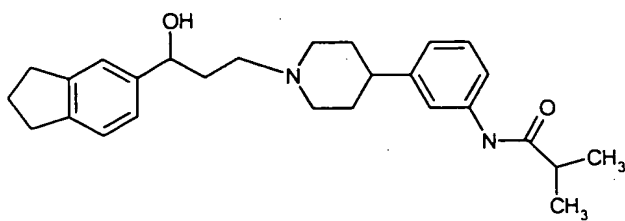
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7.2



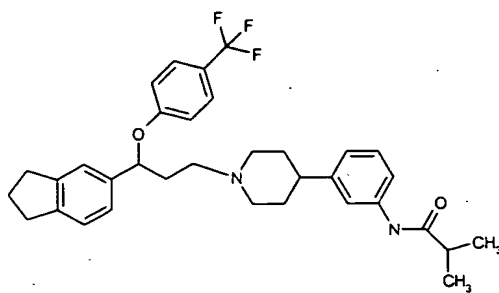
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58.3



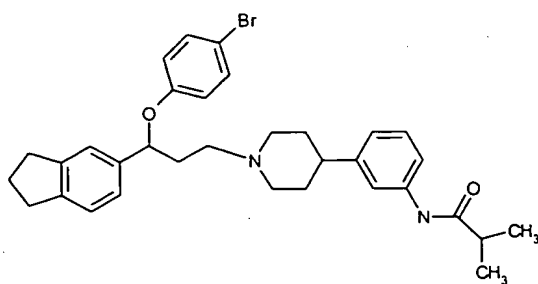
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16.3



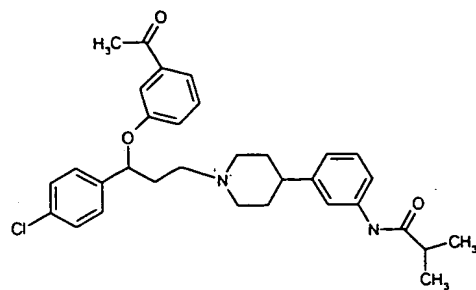
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6.2



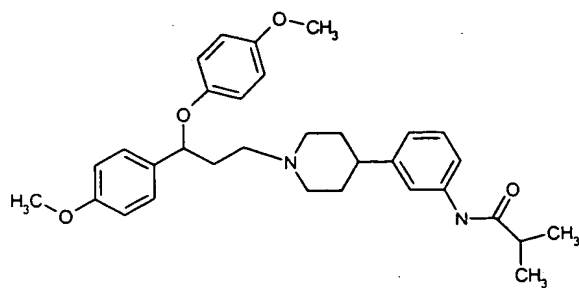
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7.7



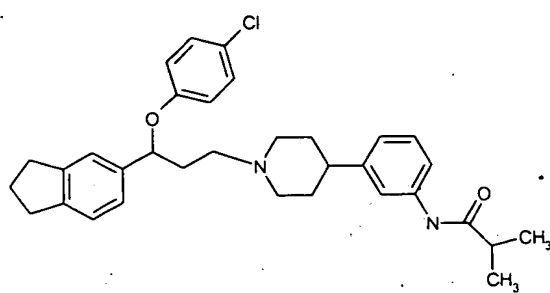
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80.4



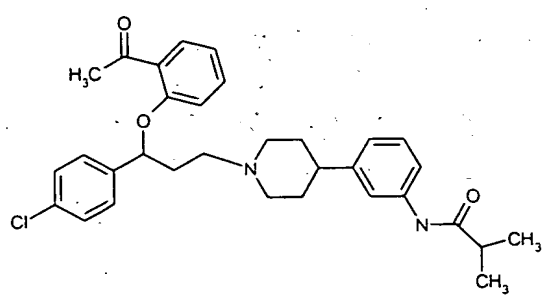
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7.0



169

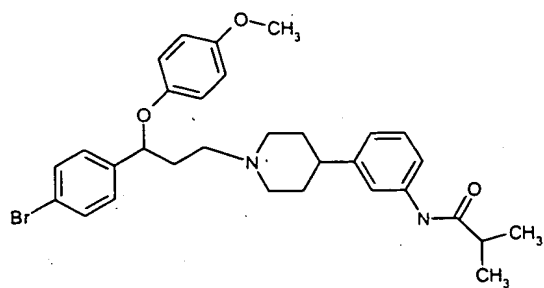
7.7



531

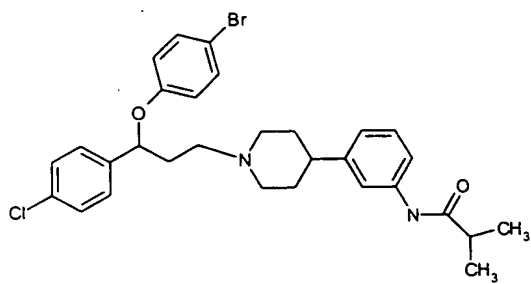
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3.0



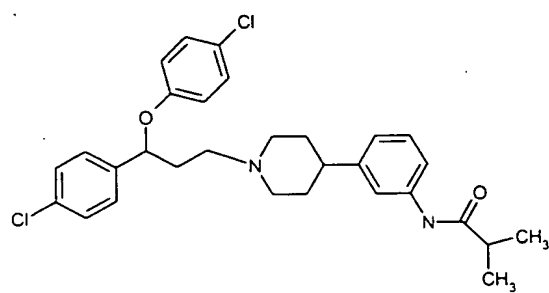
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3.7



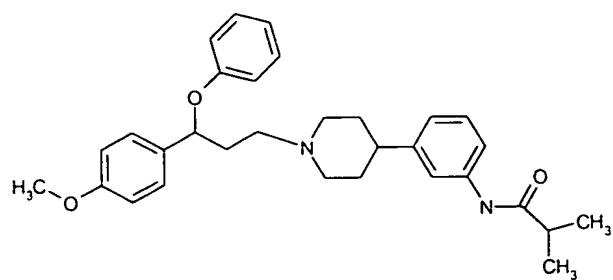
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3.0



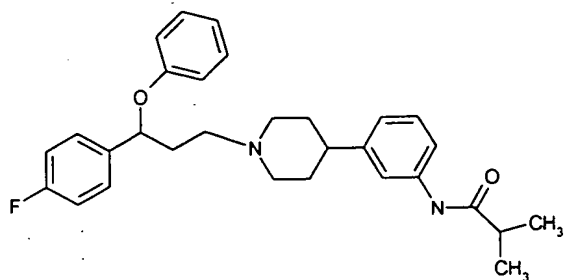
173

112.3



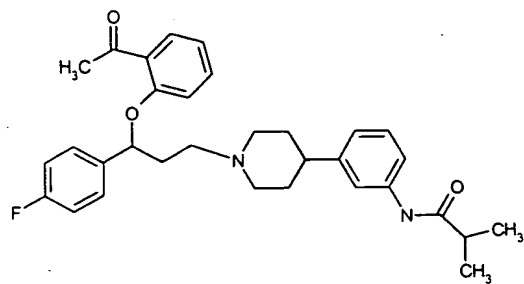
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17.0



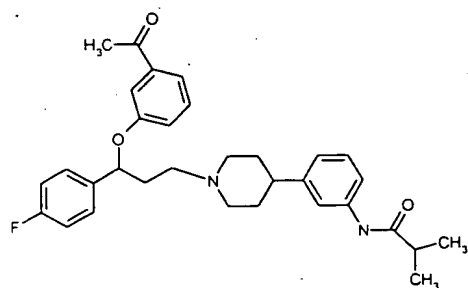
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16.2



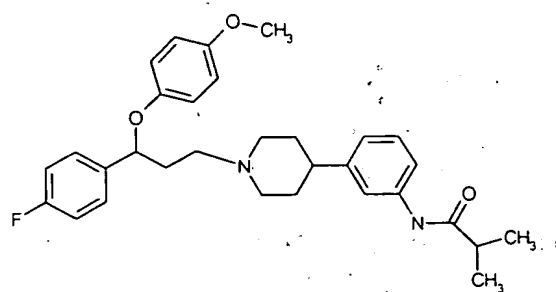
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11.8



177

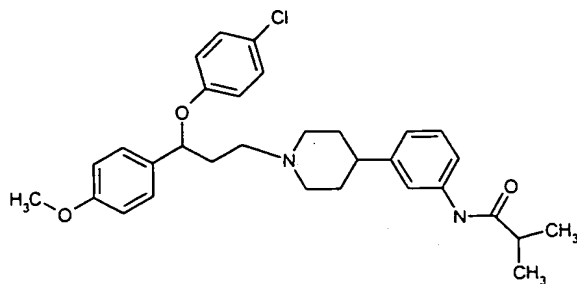
6.8



178

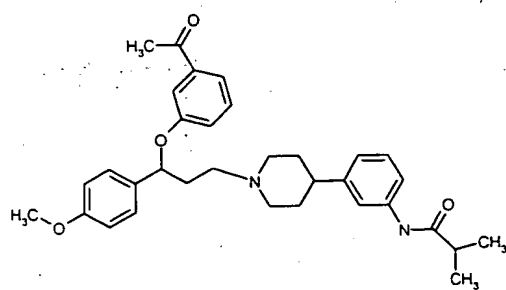
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119.2



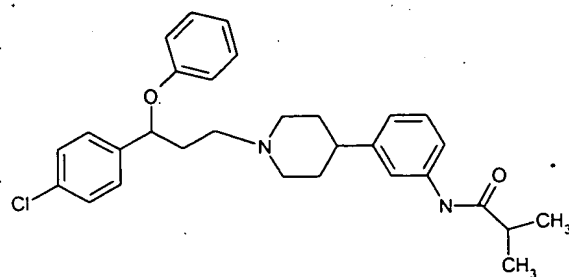
179

82.3



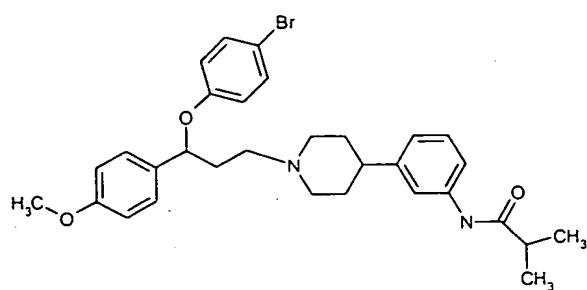
180

9.7



181

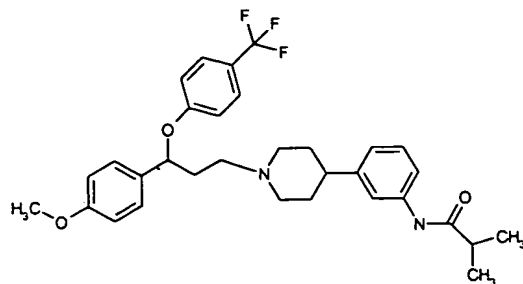
91.9



534

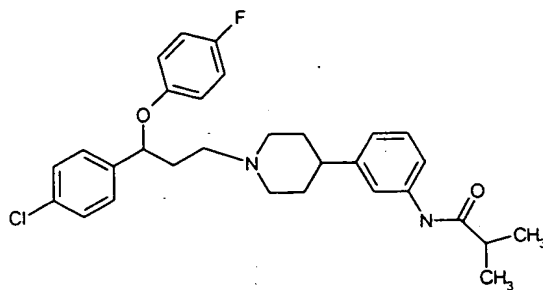
182

101.3



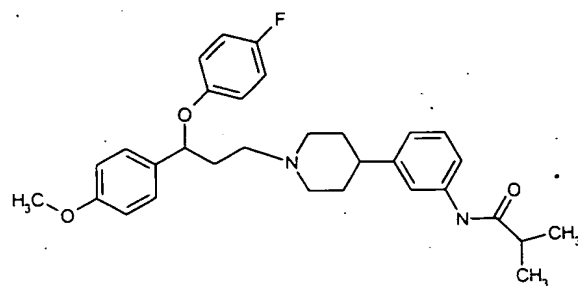
183

4.0



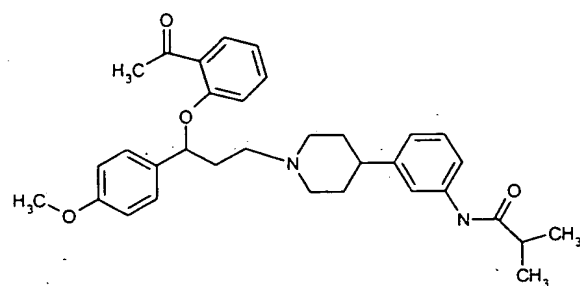
184

105.2



185

20.6

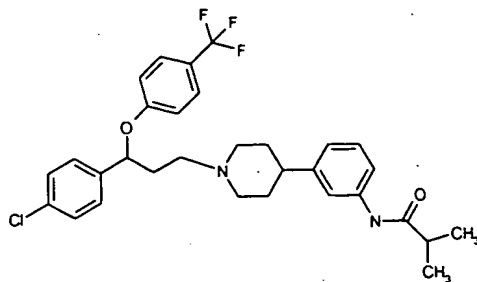




186

535

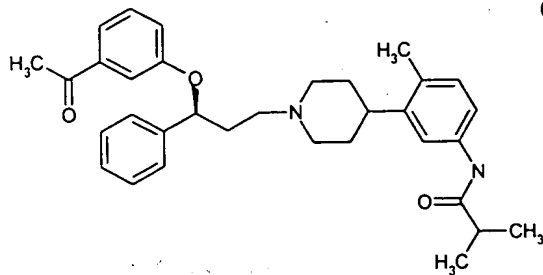
4.9



187

Chiral

15.6



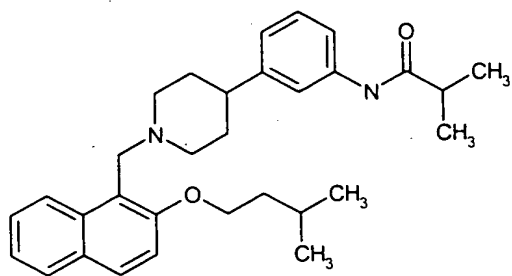
Example

Structure

rMCH1  
Ki (nM)

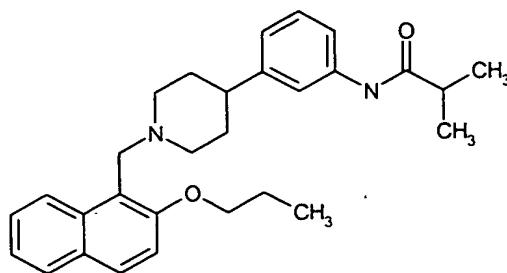
188

531.5



189

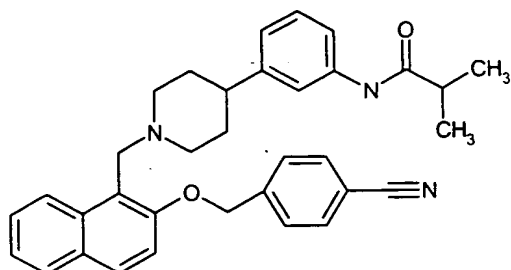
438.3



190

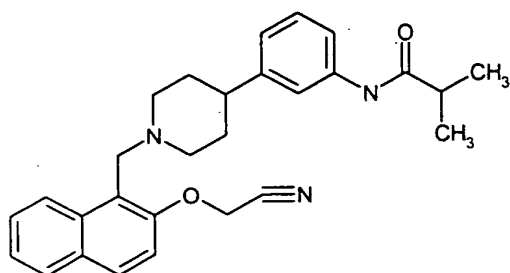
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435.6



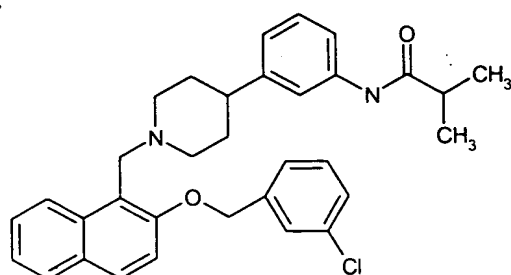
191

648.7



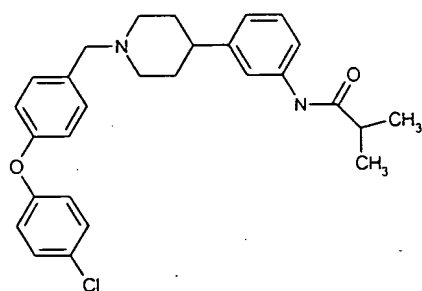
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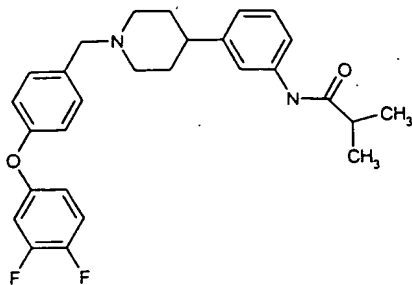
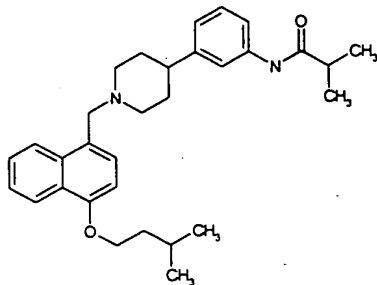
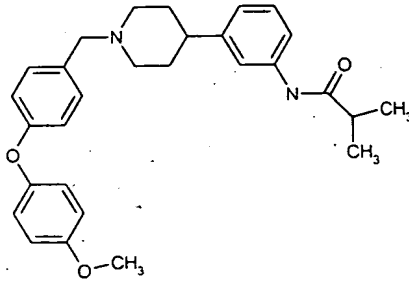
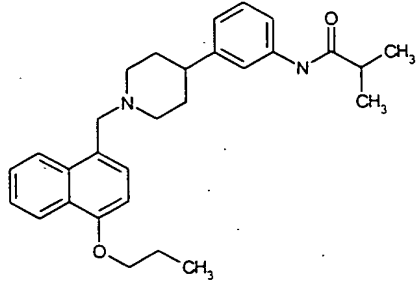
80.5



193

5.2

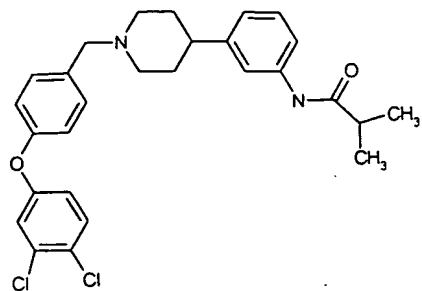


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195		106.0
		
196		35.2
		
197		63.1
		

538

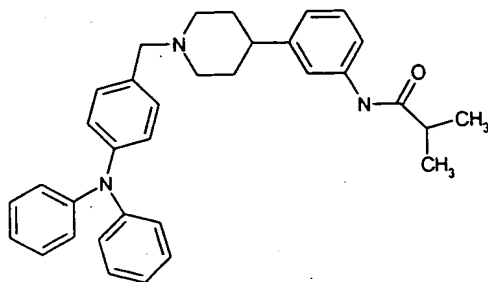
198

6.1



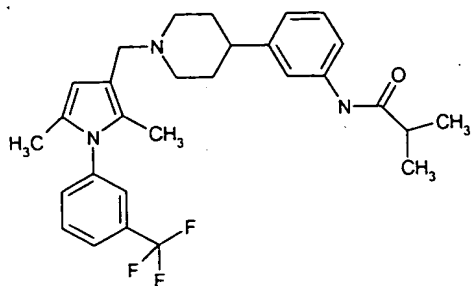
199

3.6



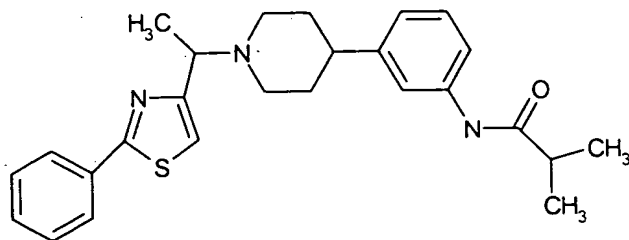
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20.9

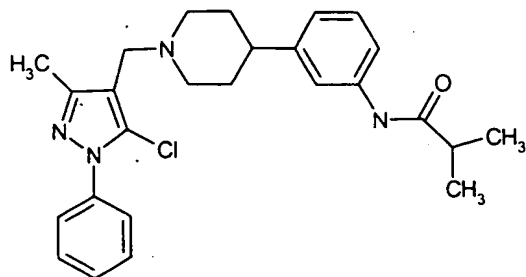


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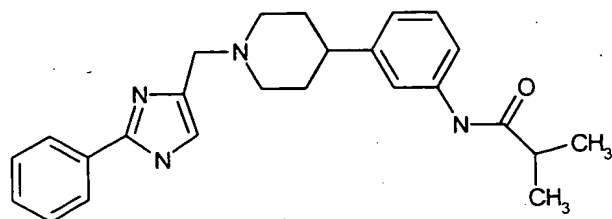
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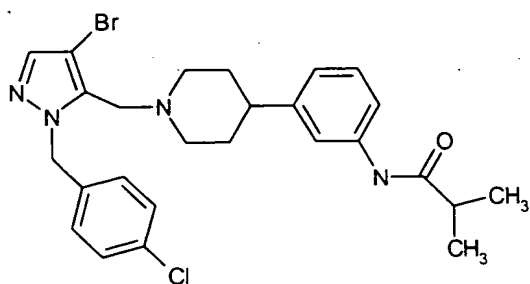
202 539 154.7



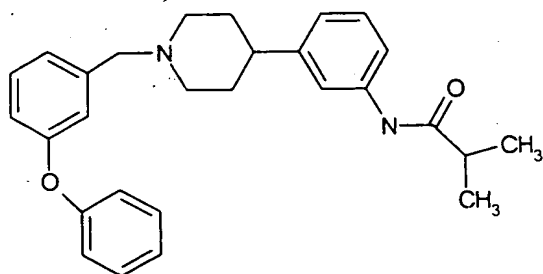
203 79.6



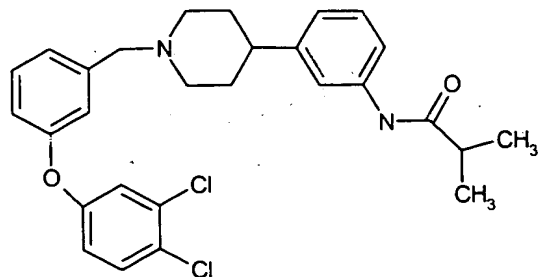
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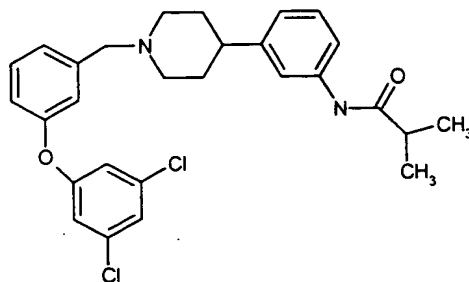
205 28.0



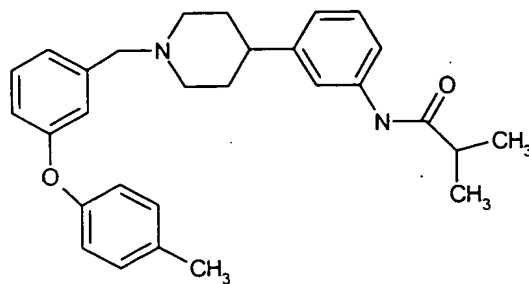
206 540 17.7



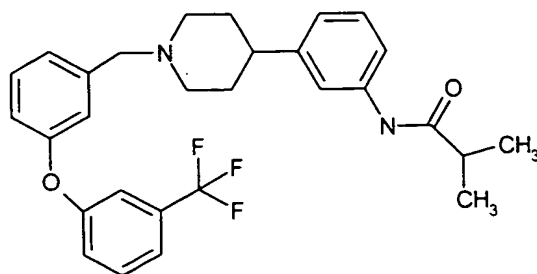
207 136.8

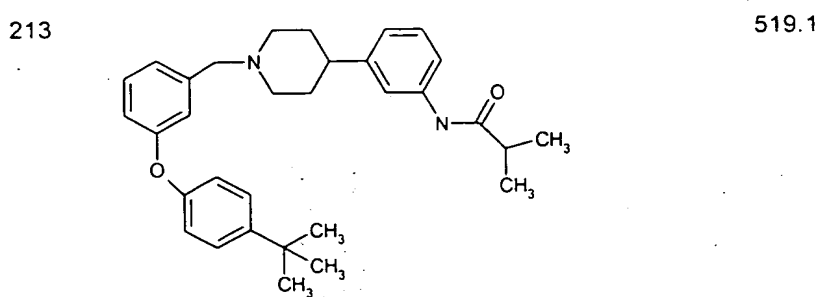
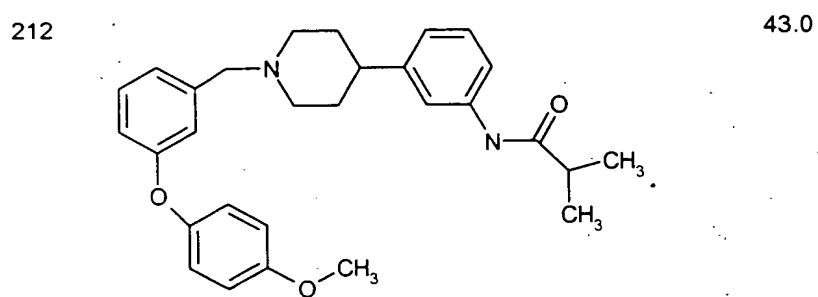
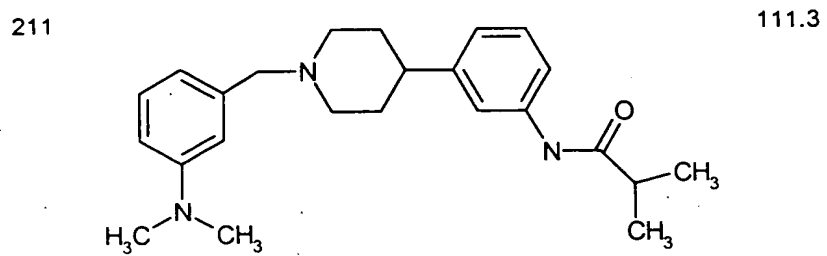
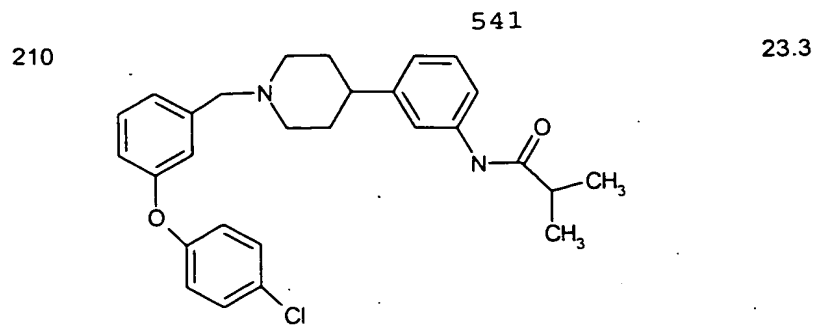


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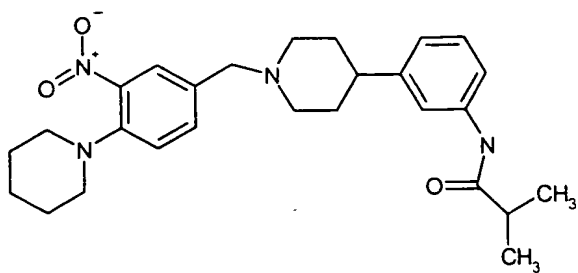


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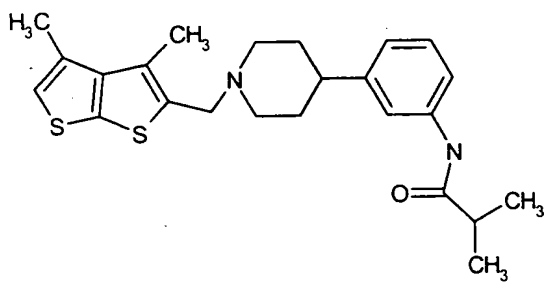




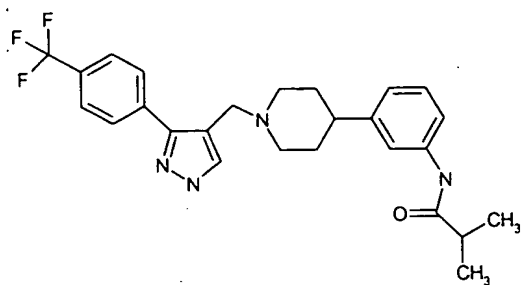
214 542 56.3



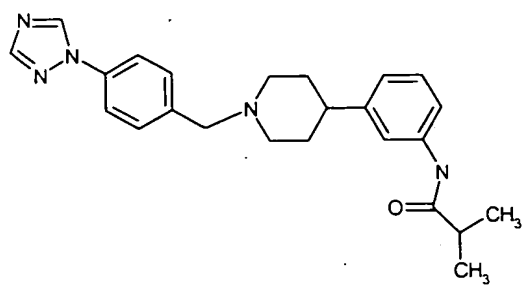
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216 817.9

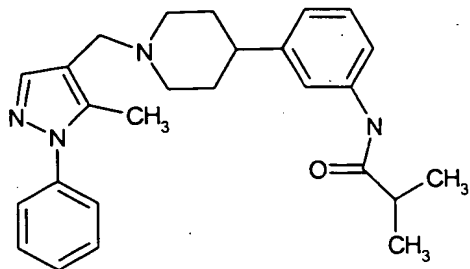


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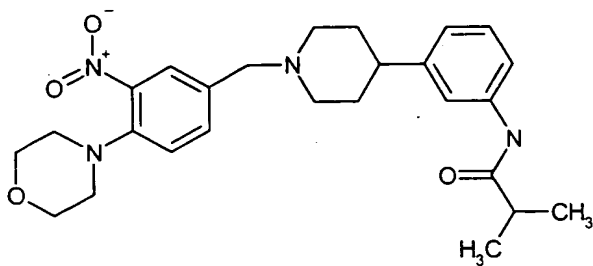




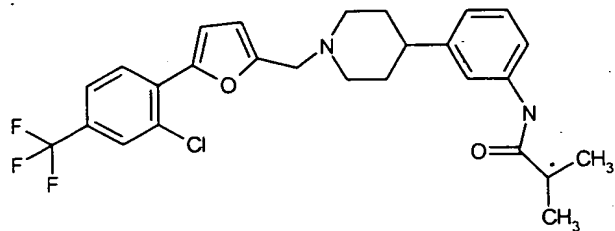
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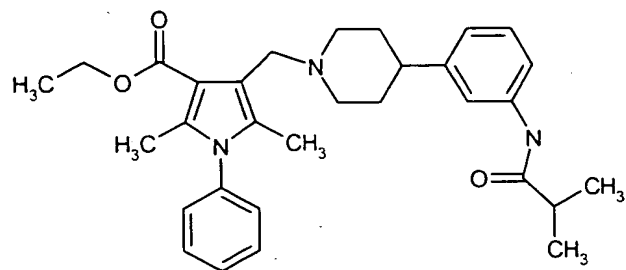
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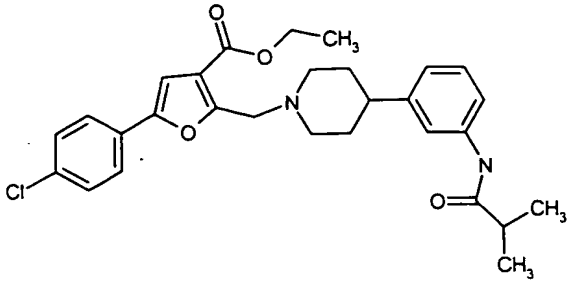
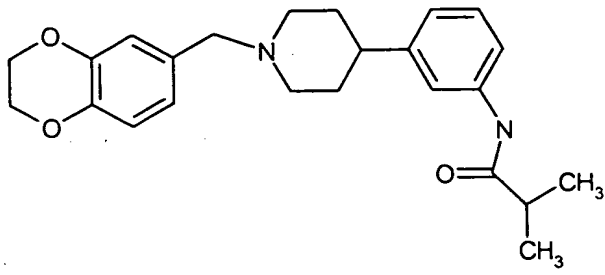
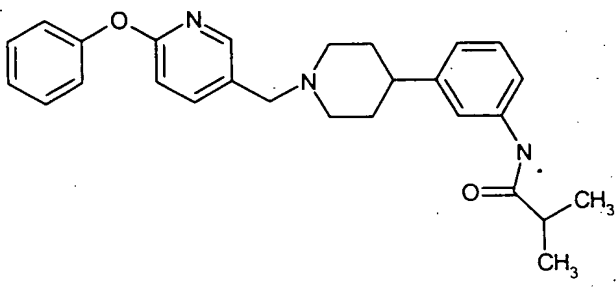
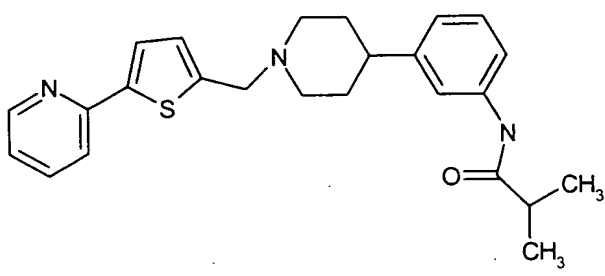


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221 545.7

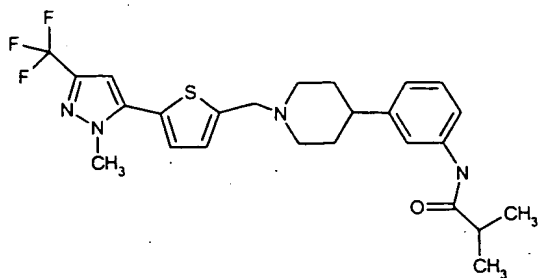


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223		318.2	
224		48.0	
225		213.6	

545

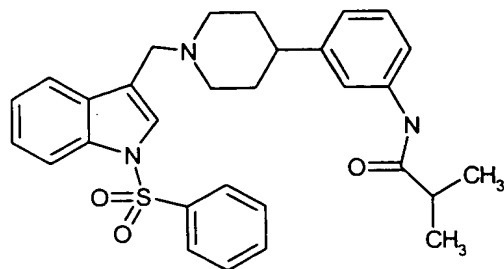
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238.8



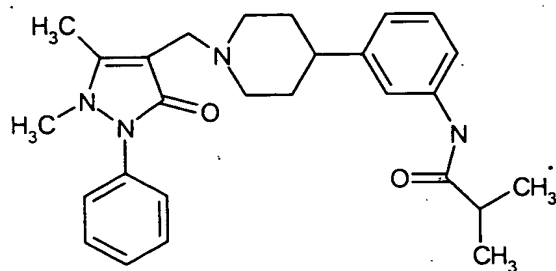
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261.6



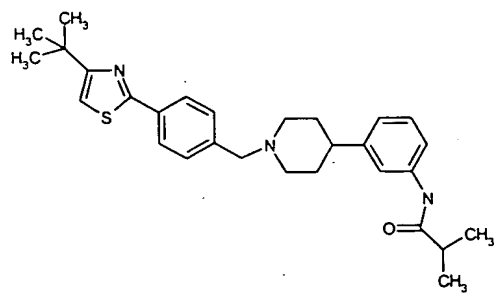
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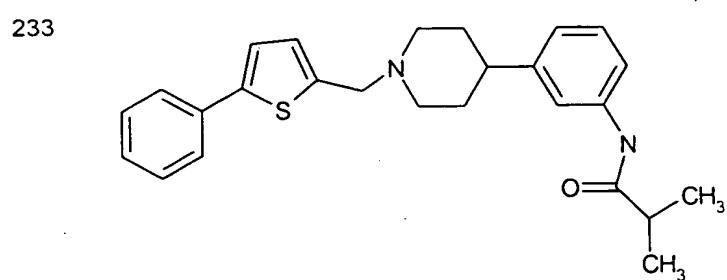
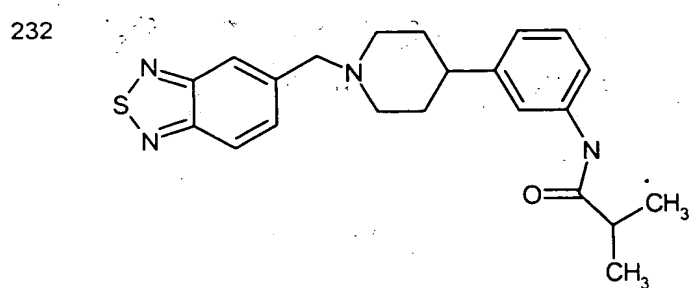
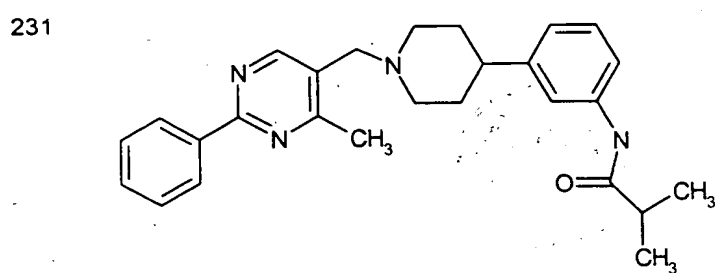
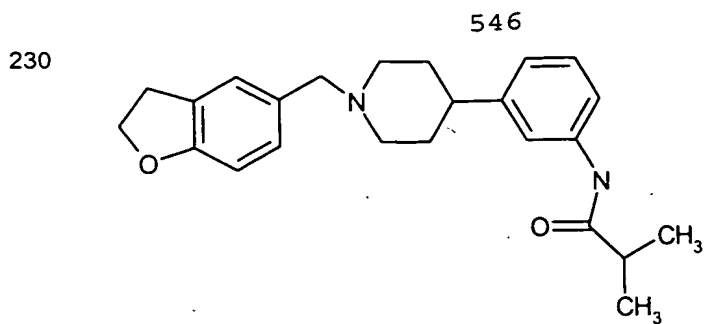
841.1



229

884.5

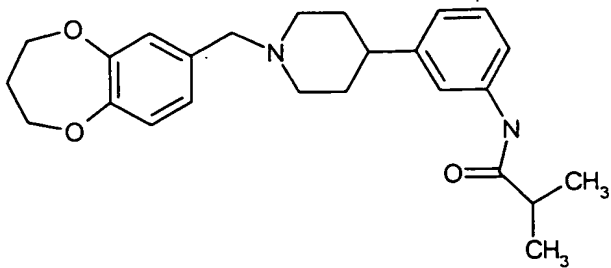




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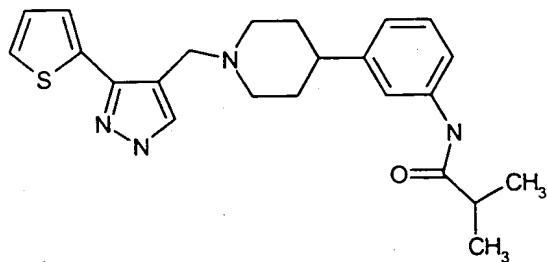
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116.1



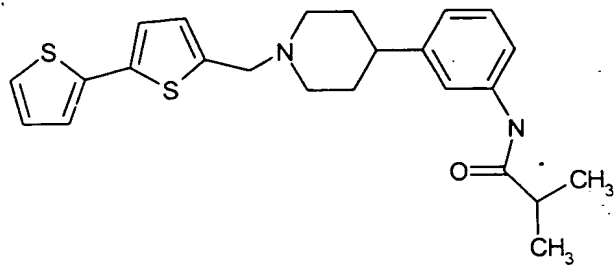
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411.7

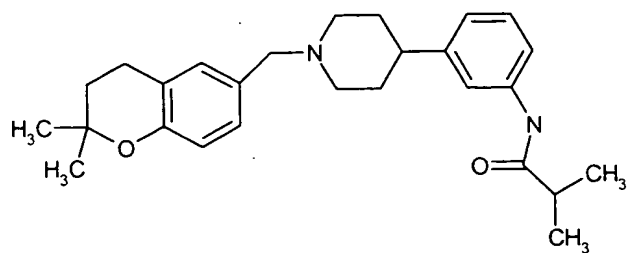


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97.7



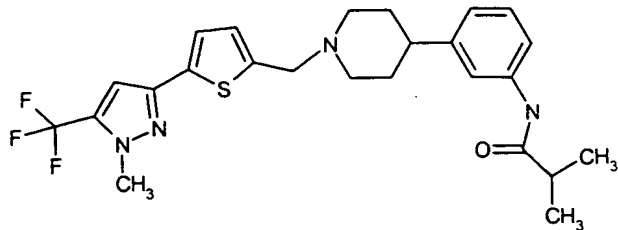
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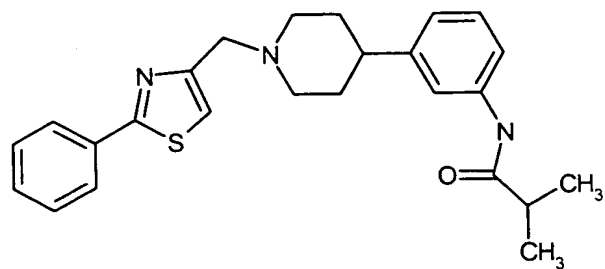
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548

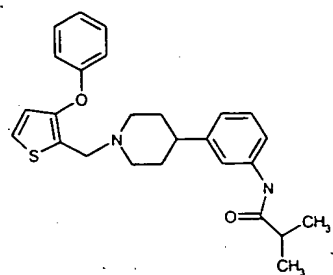
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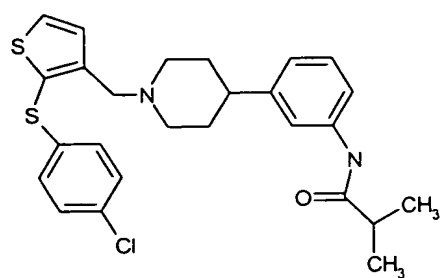
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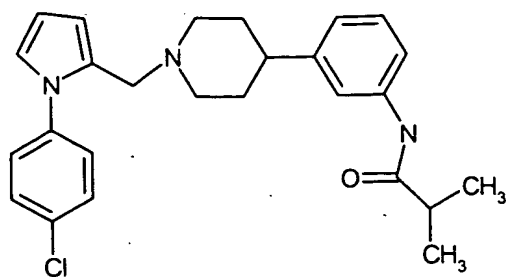


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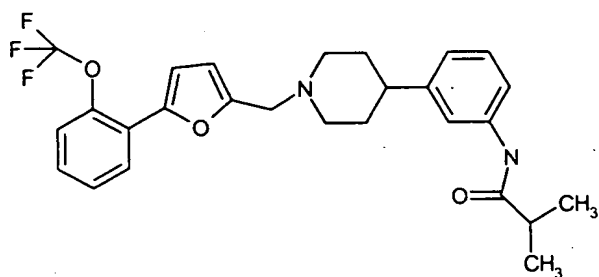


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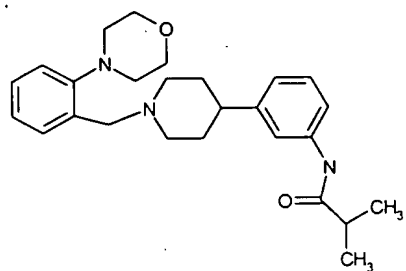
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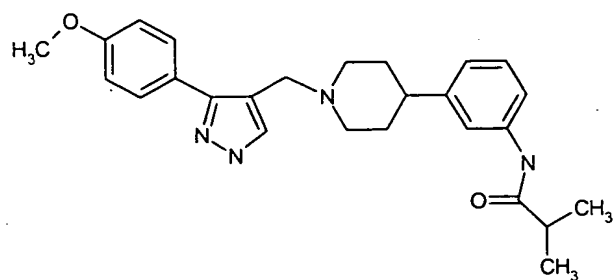
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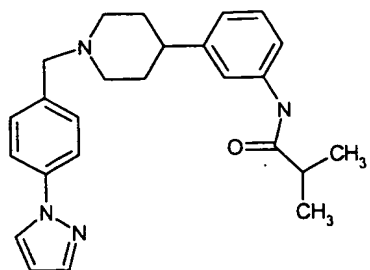
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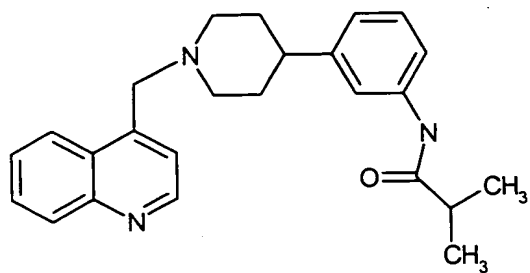
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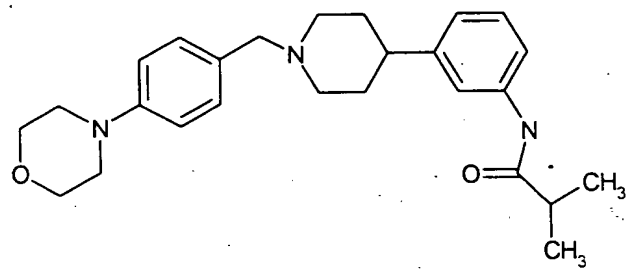
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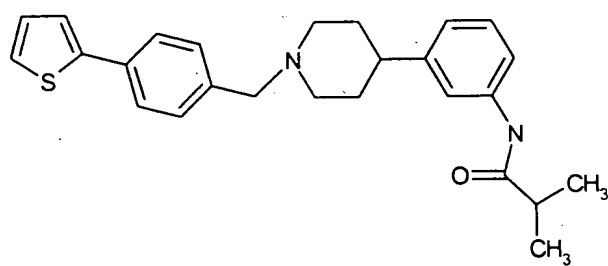
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248

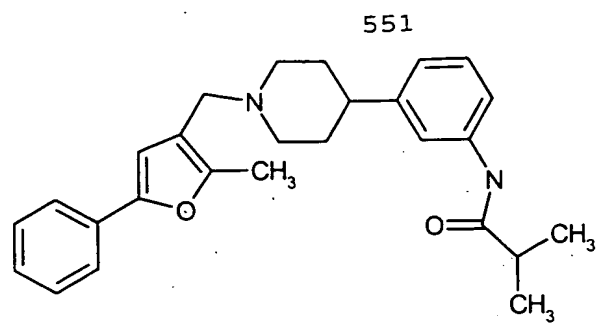


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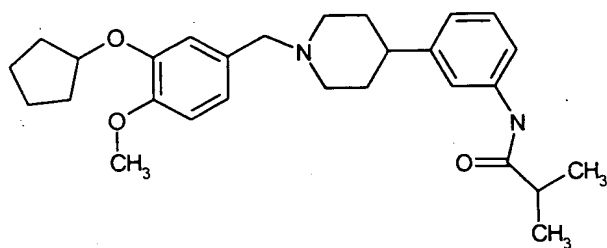




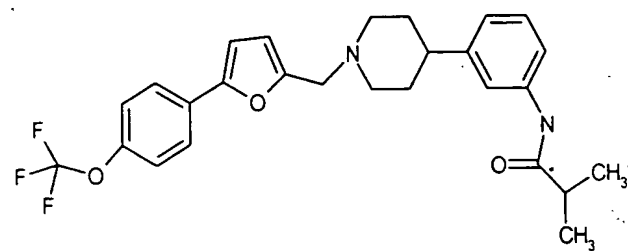
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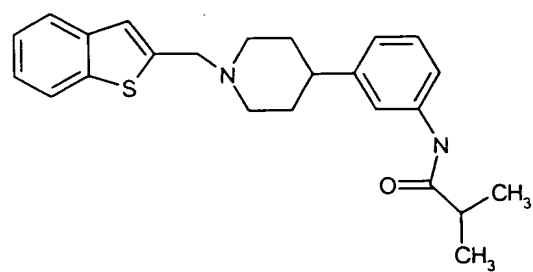
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252



253

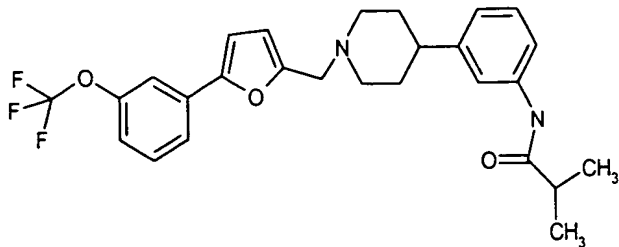


361.6

254

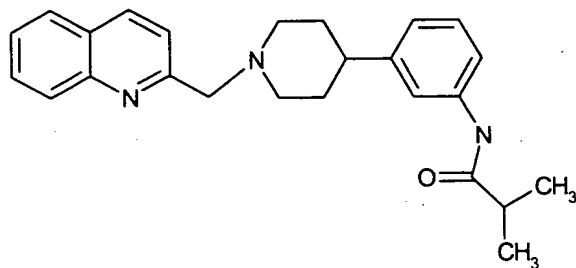
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400.7



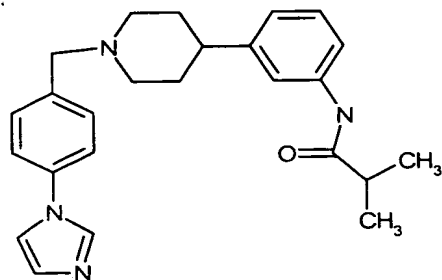
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589.8



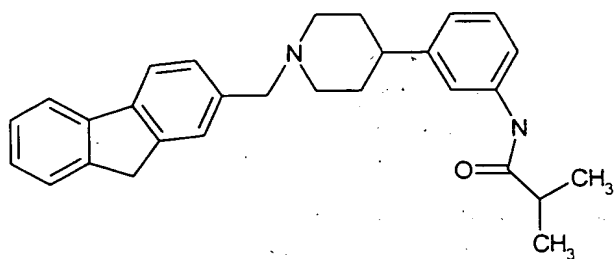
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320.5



257

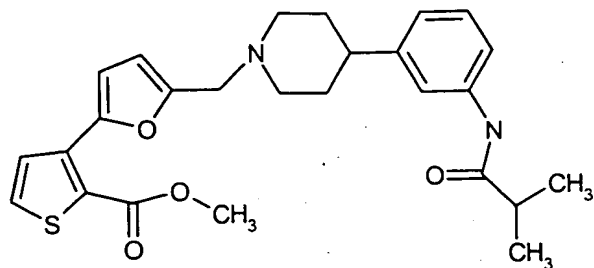
37.2



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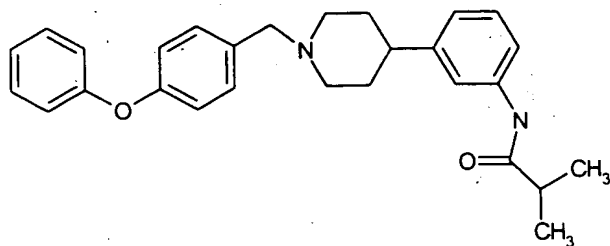
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110.3



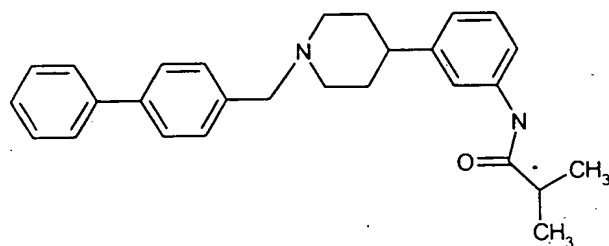
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15.4



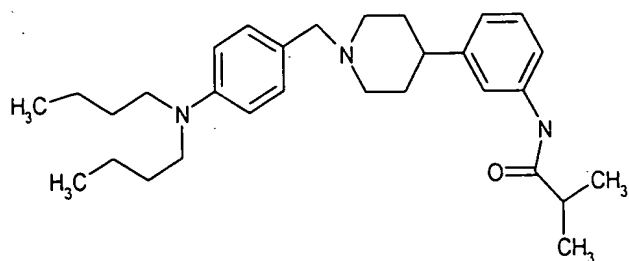
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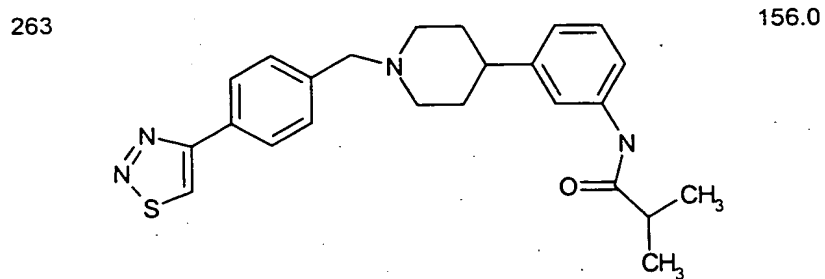
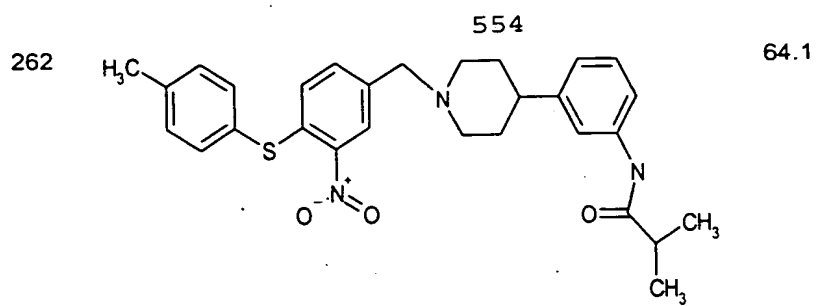
77.7



261

6.5

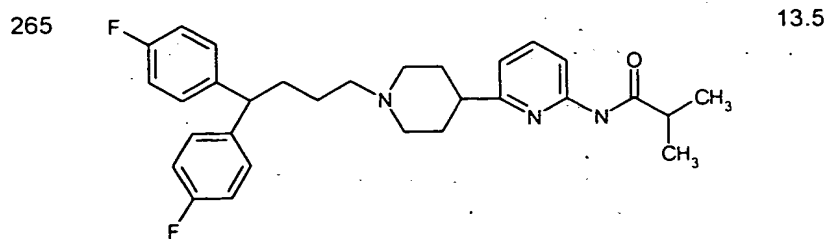
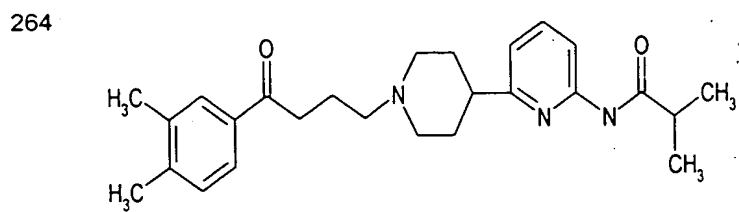




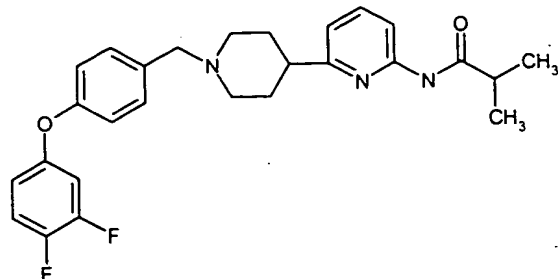
Example

Structure

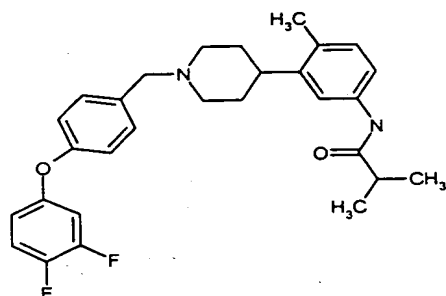
rMCH-1  
Ki (nM)



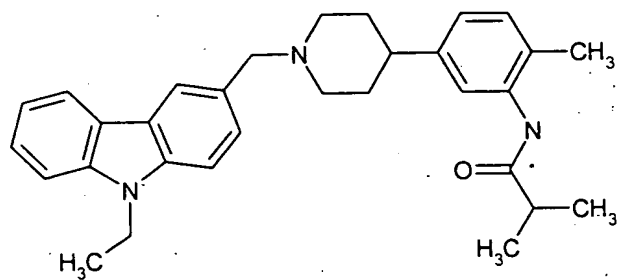
266 555 6.4



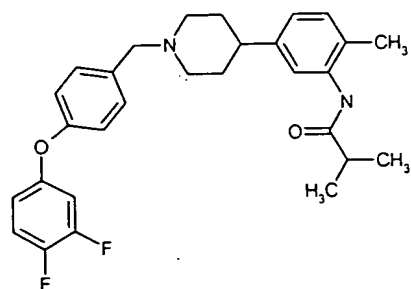
267 2.2



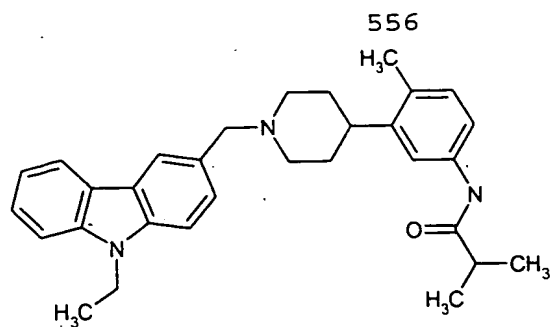
268 20.3



269 27.4

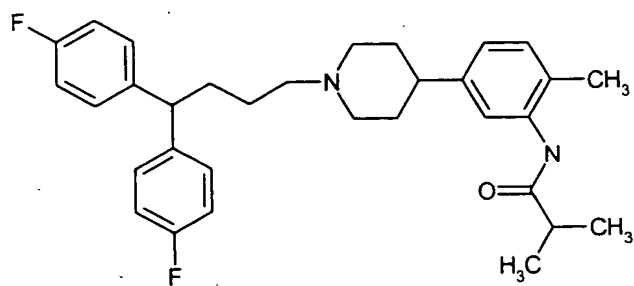


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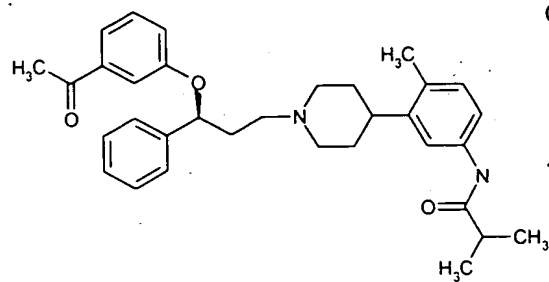
3.4

271



40.1

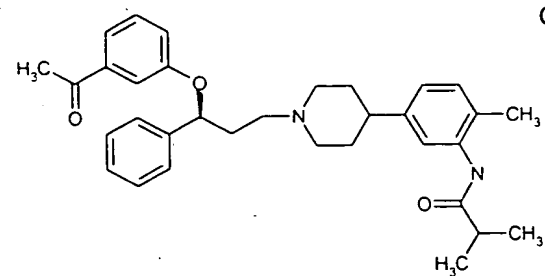
272



Chiral

15.6

273

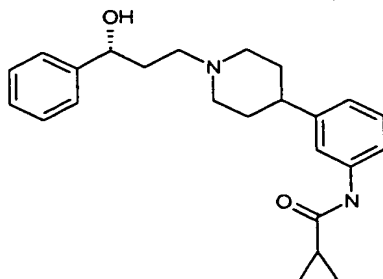


Chiral

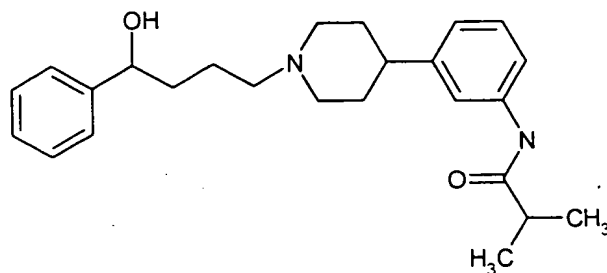
196.4

[illegible]

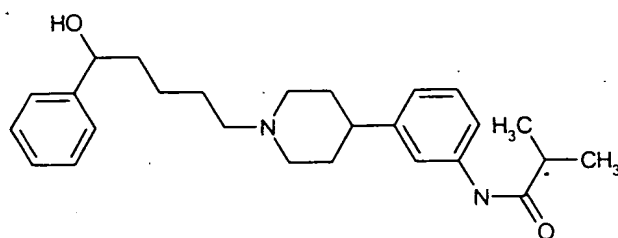
278 558  
Chiral 85.8



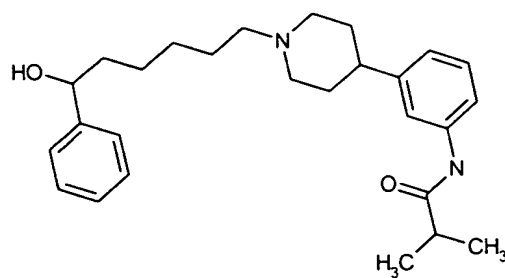
279 74.5



280 27.6

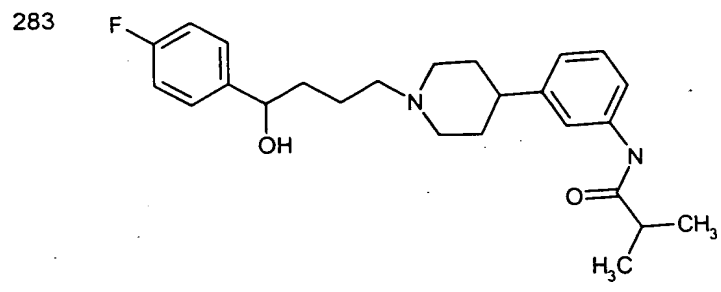
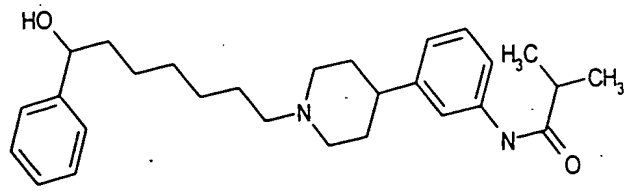


281 7.9

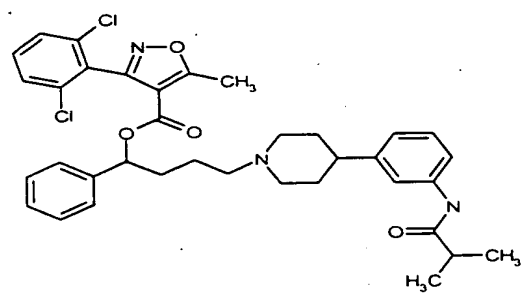




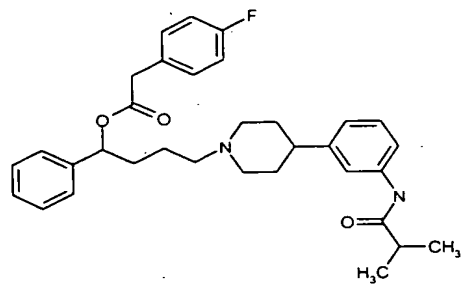
282 559 23.5



284 16.3

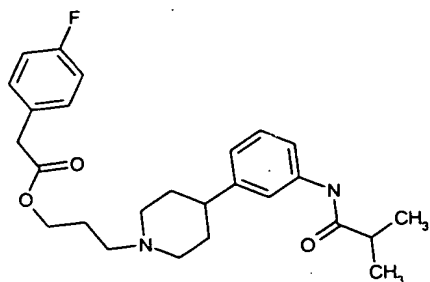


285 10.3



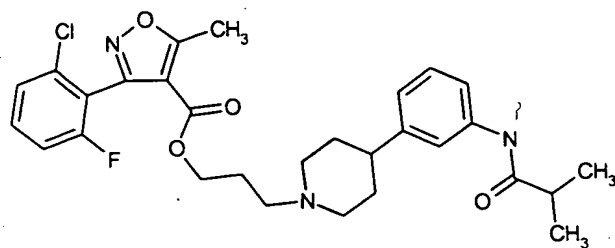
286

67.8



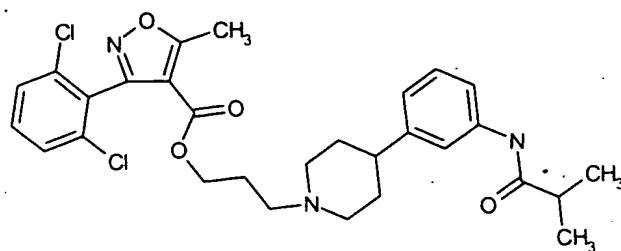
287

34.3



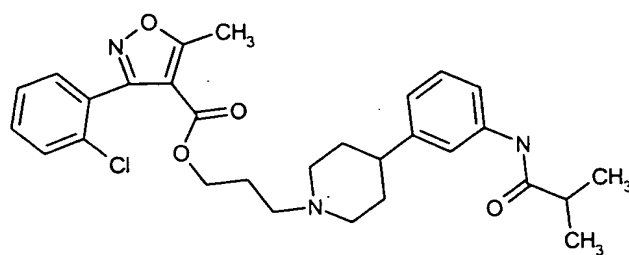
288

30.2

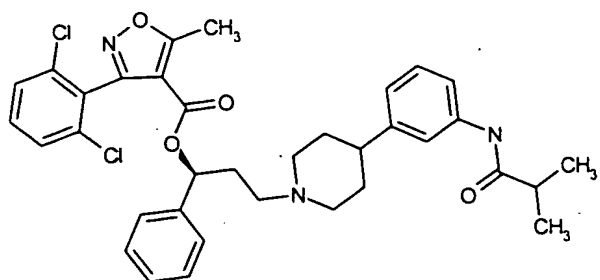


289

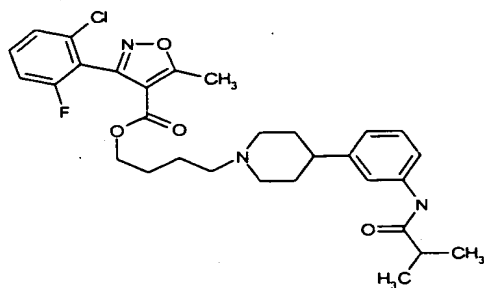
31.8



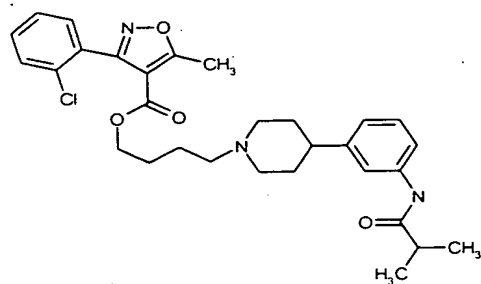
290 561 51.9



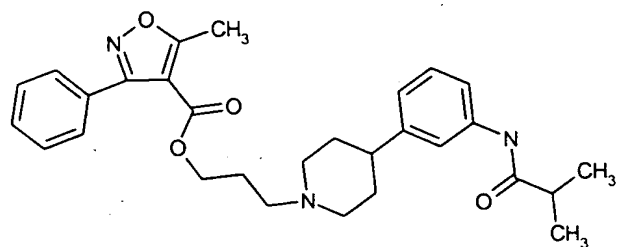
291 24.3



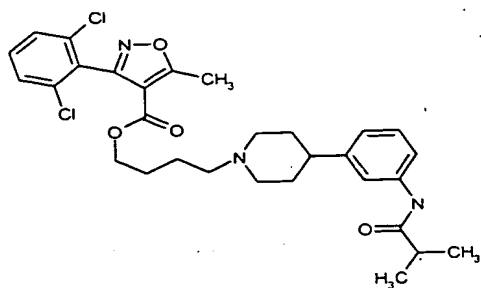
292 18.4



293 39.9

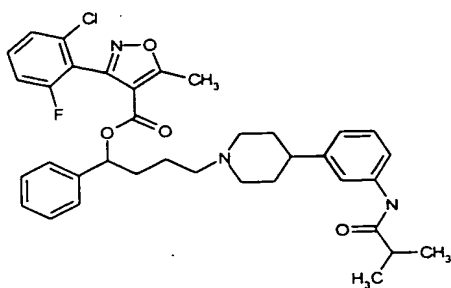


294



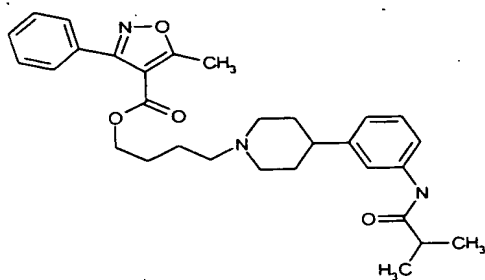
8.7

295



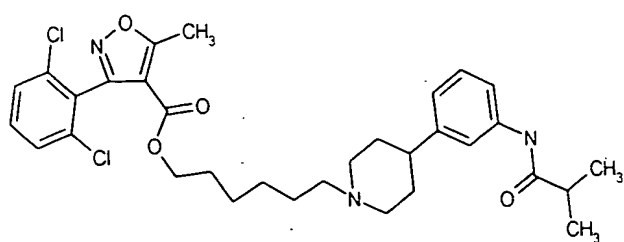
20.0

296



11.9

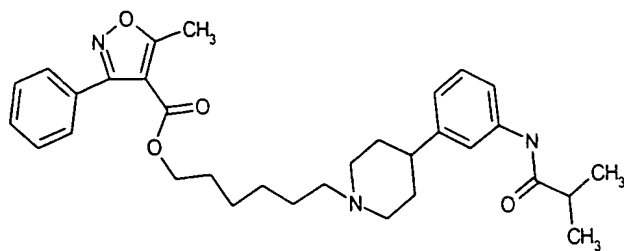
297



563

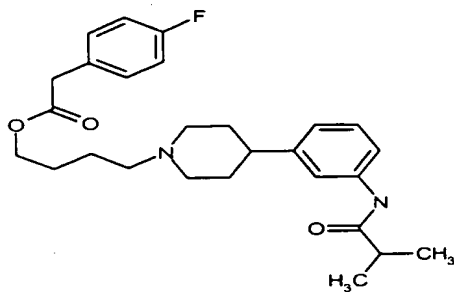
298

40.1



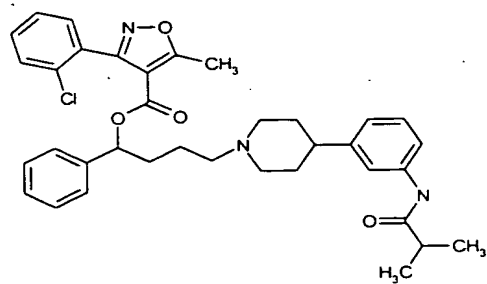
299

37.5

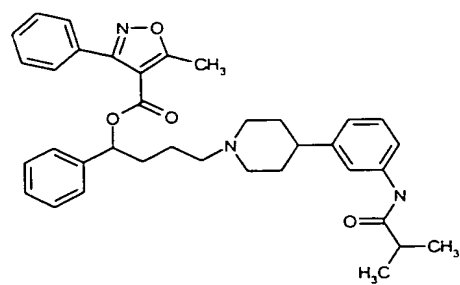


300

7.6



301

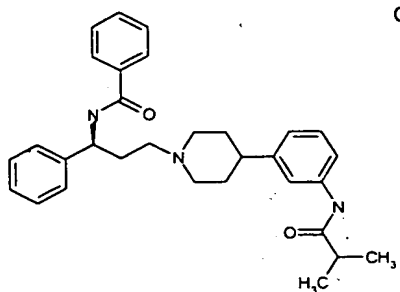


302

564

Chiral

20.5



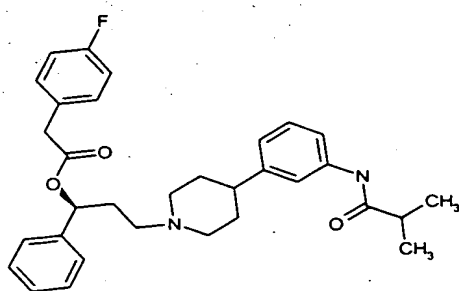
Example

Structure

rMCH-1  
Ki (nM)

303

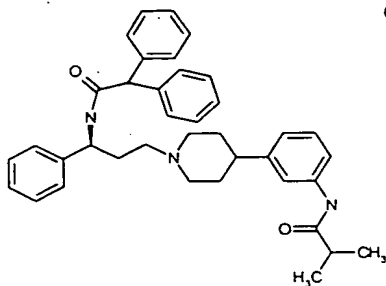
9.5



304

Chiral

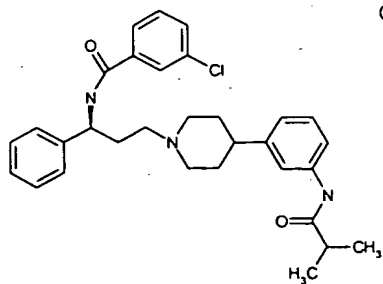
4.0

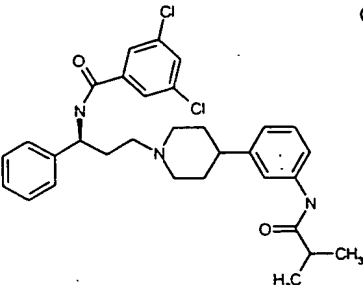
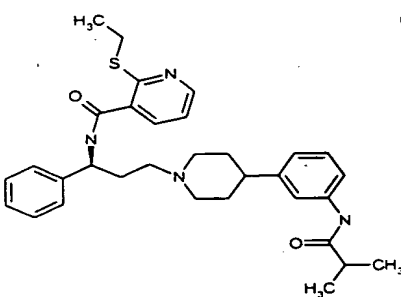
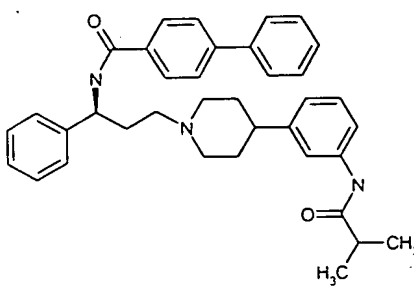
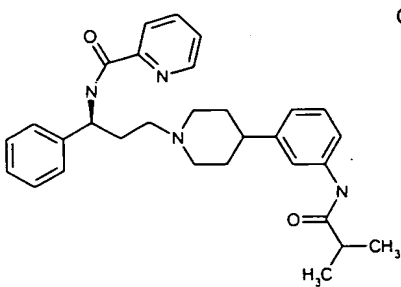


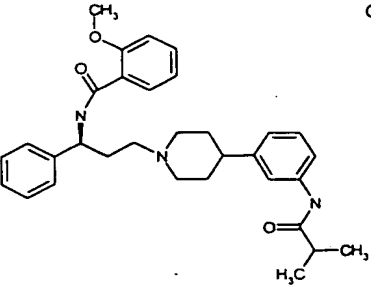
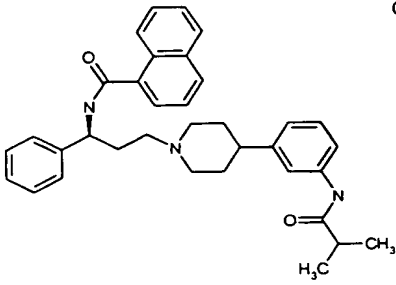
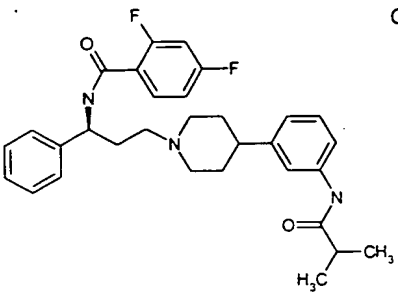
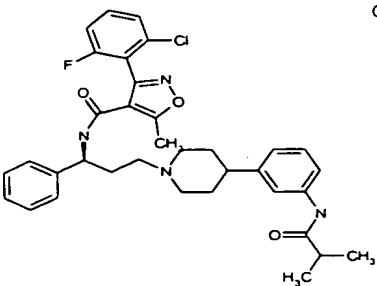
305

Chiral

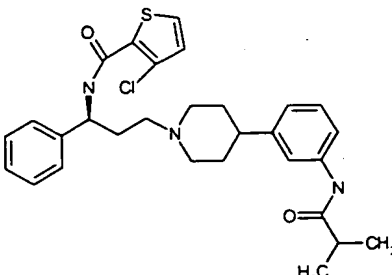
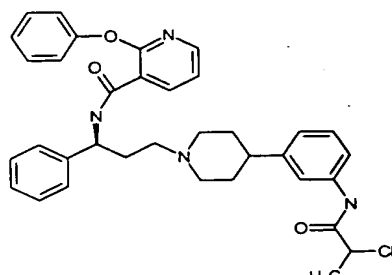
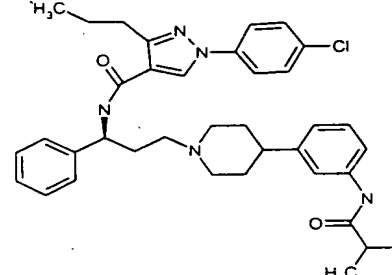
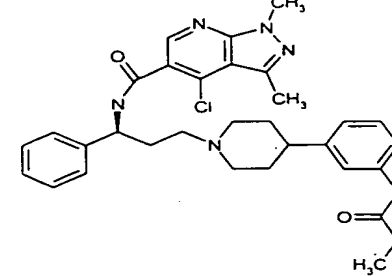
177.2

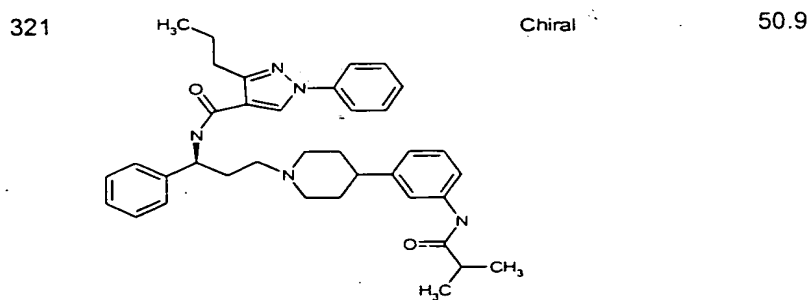
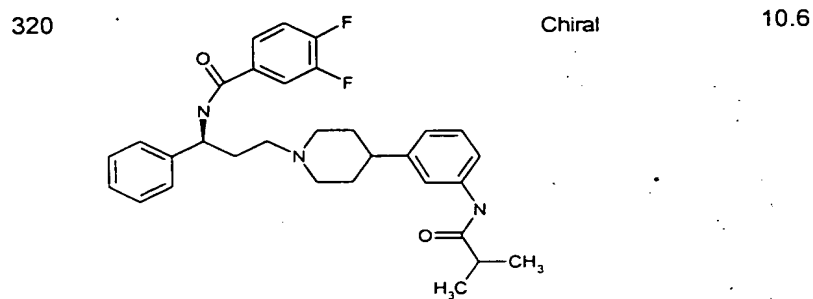
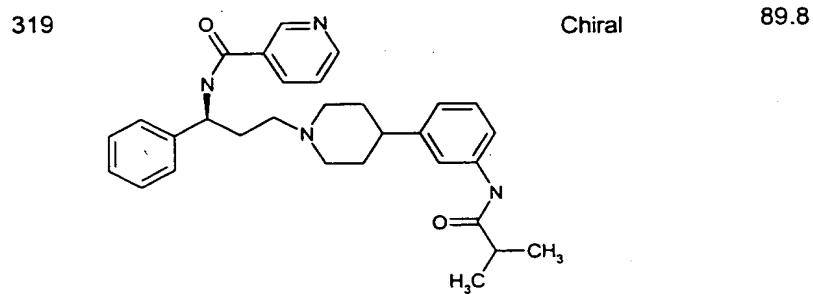
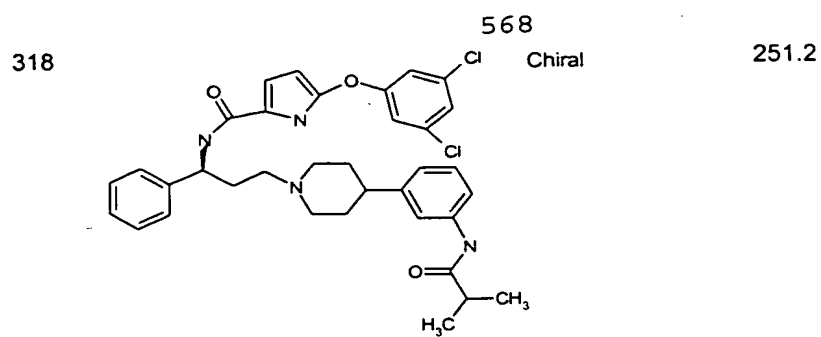


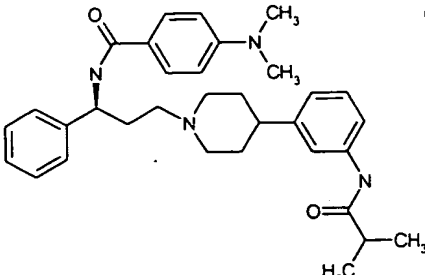
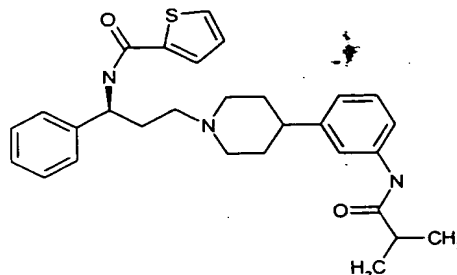
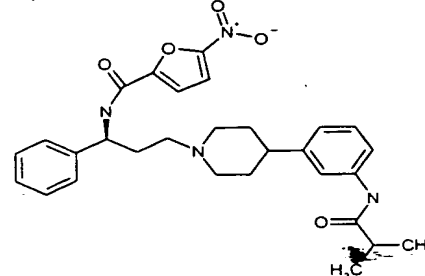
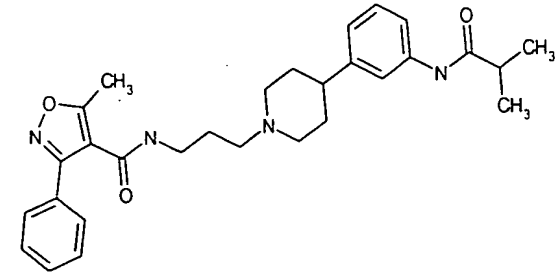
306		565 Chiral	167.9
307		Chiral	97.4
308		Chiral	401.6
309		Chiral	310.1

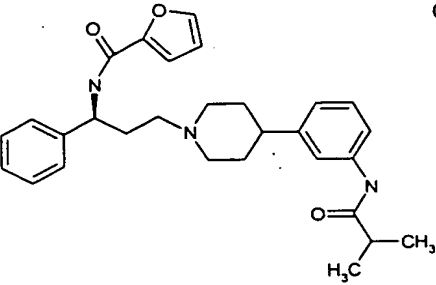
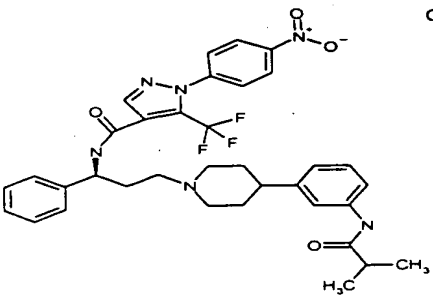
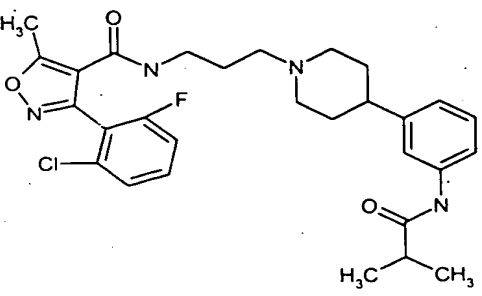
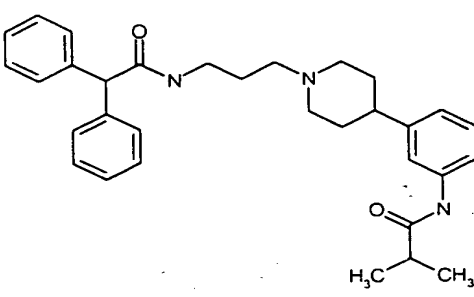
310		566 Chiral	152.2
311		Chiral	43.0
312		Chiral	61.5
313		Chiral	249.3



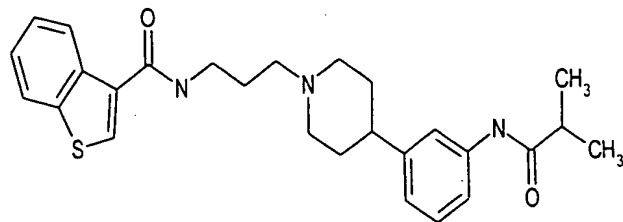
314		567 Chiral	7.6
315		Chiral	11.4
316		Chiral	8.3
317		Chiral	110.2



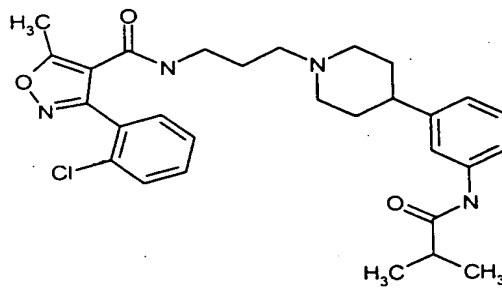
322		569 Chiral	99.9
323		Chiral	37.0
324		Chiral	76.8
325			29.8

326		570 Chiral	19.2
327		Chiral	7.7
328			47.6
329			2.9

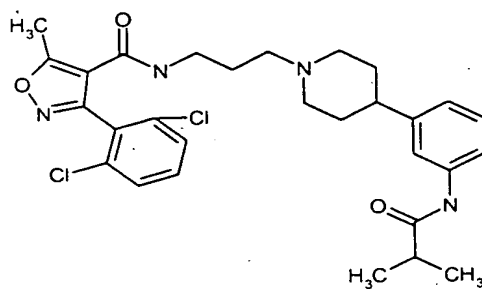
330 571 215.0



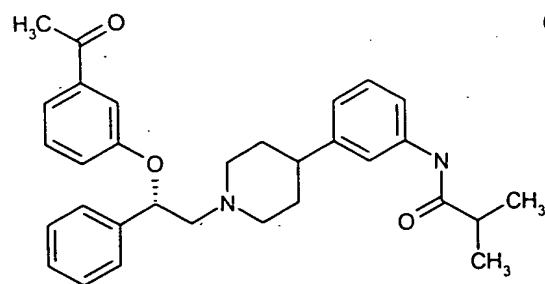
331 51.3



332 29.0



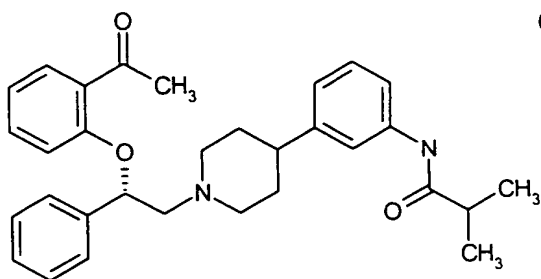
Example	Structure	rMCH-1 Ki (nM)
333	Chiral	567.8



334

Chiral

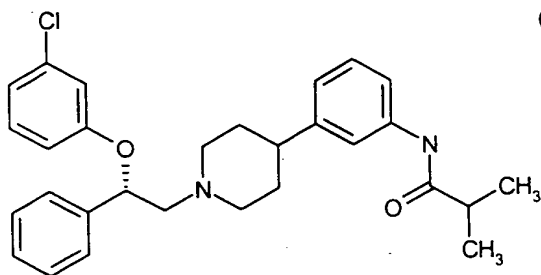
602.8



335

Chiral

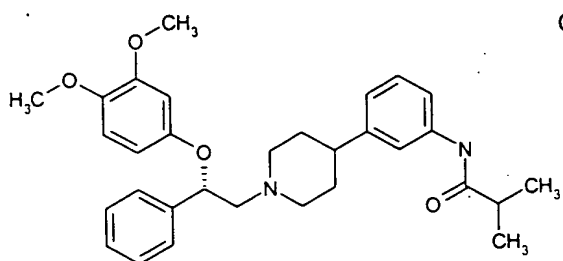
887.7



336

Chiral

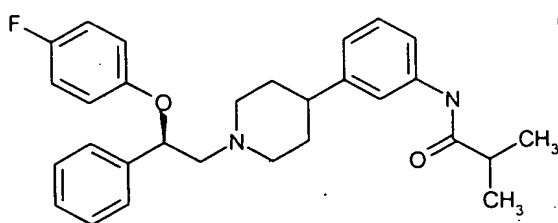
693.0



337

Chiral

907.4

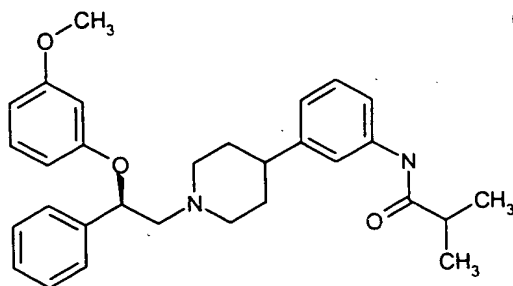


573

338

Chiral

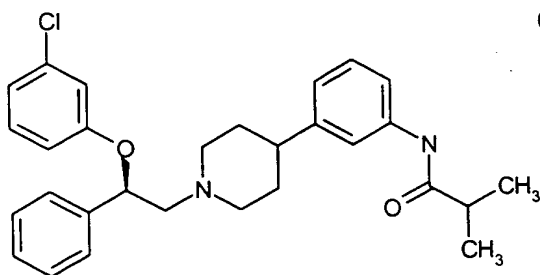
843.9



339

Chiral

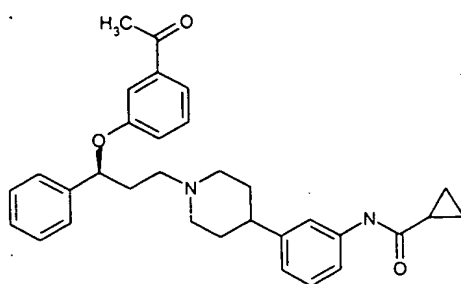
889.9



340

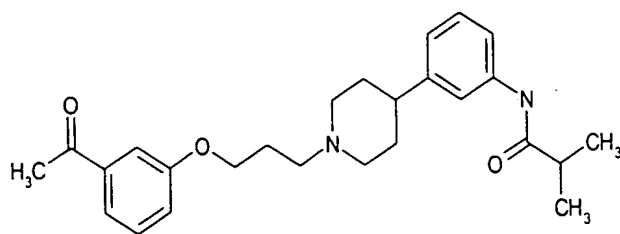
Chiral

15.6



341

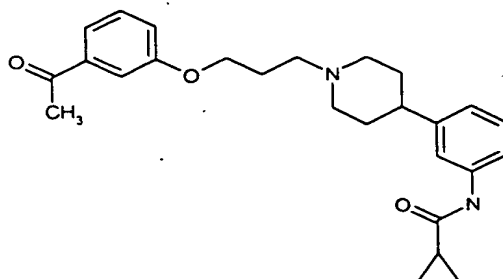
255.6



574

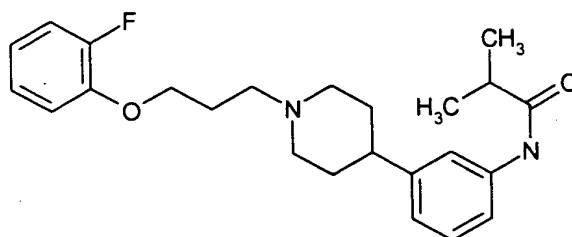
342

183.0



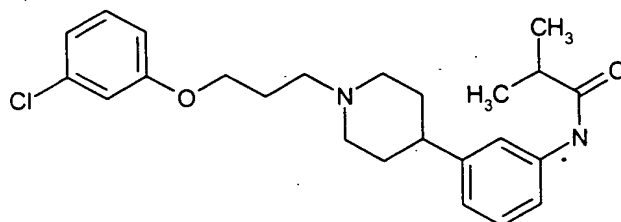
343

194.7



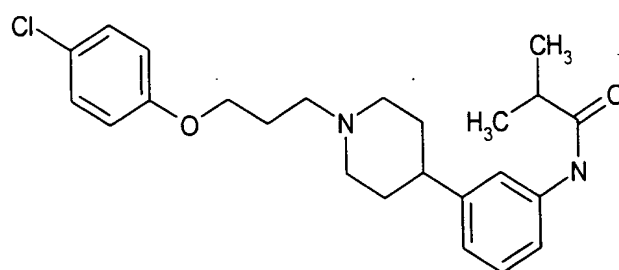
344

44.6



345

15.4

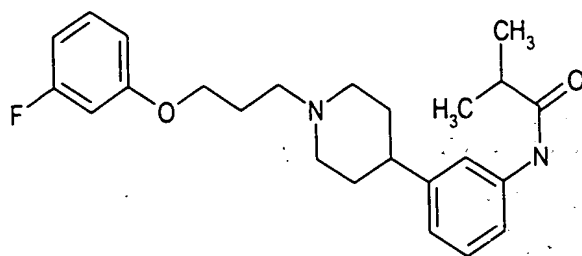




575

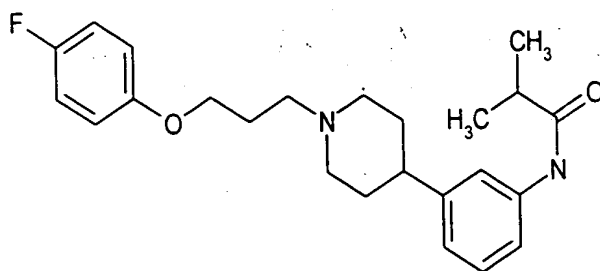
346

106.9



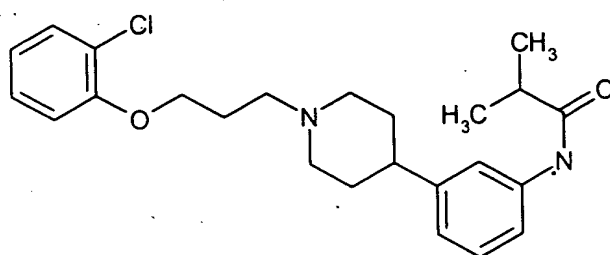
347

54.8



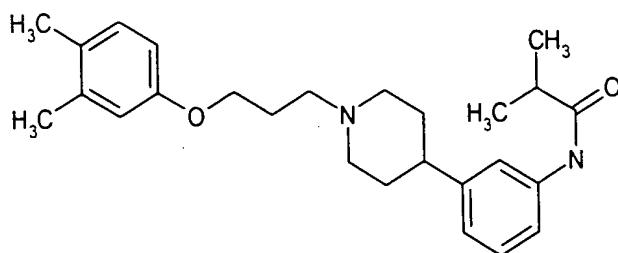
348

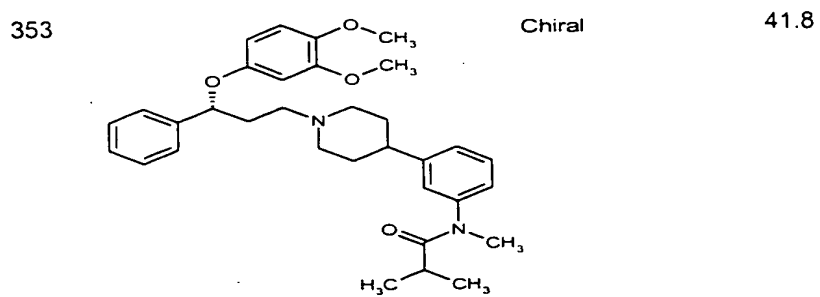
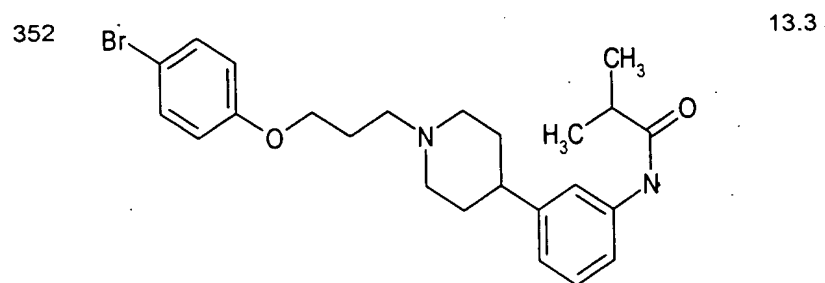
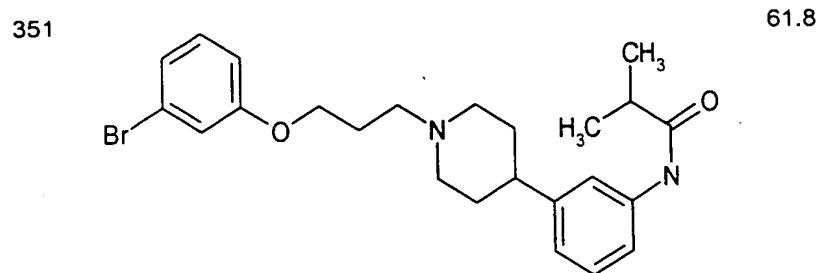
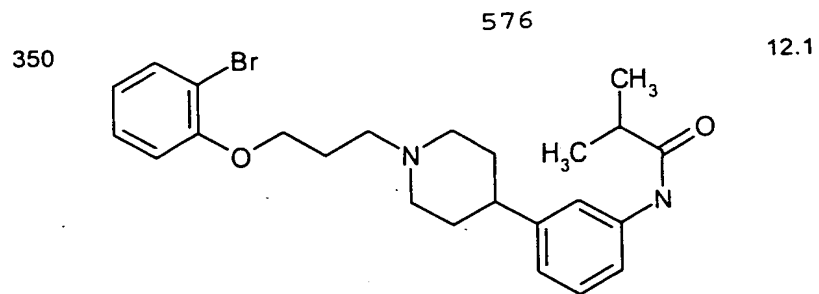
84.0



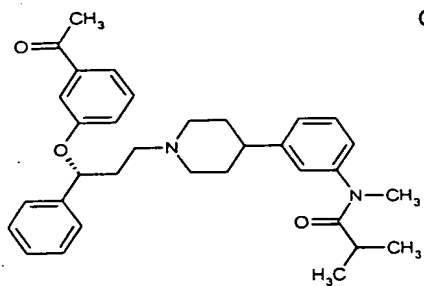
349

20.4

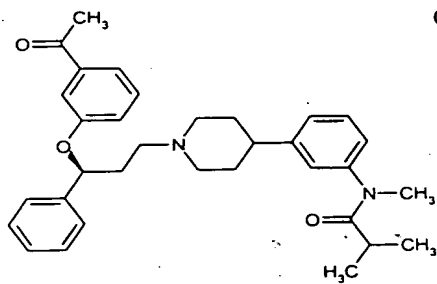




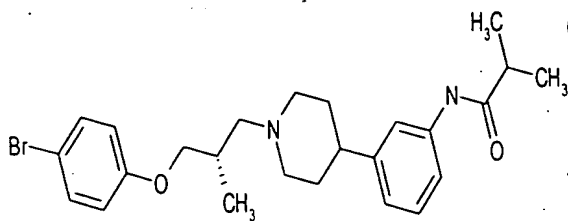
354 577 Chiral 81.6



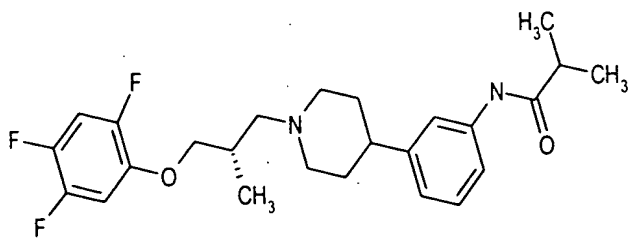
355 Chiral 116.6

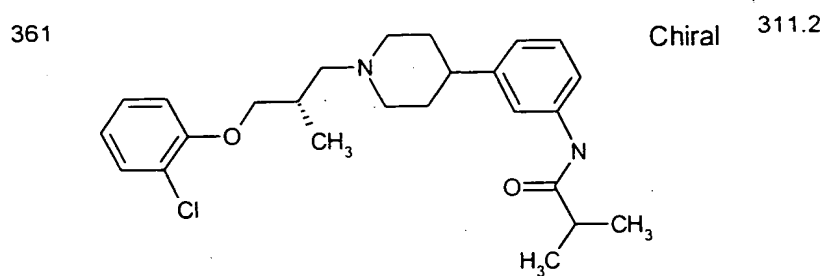
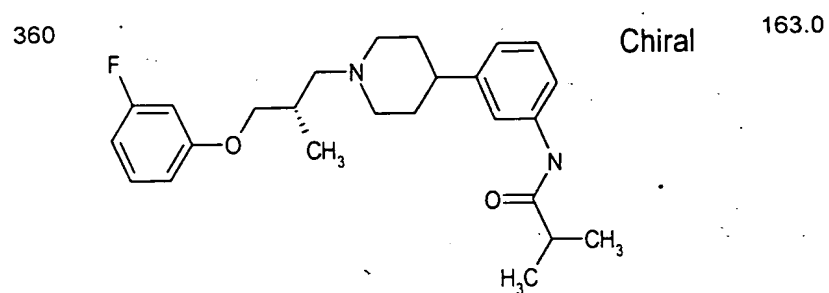
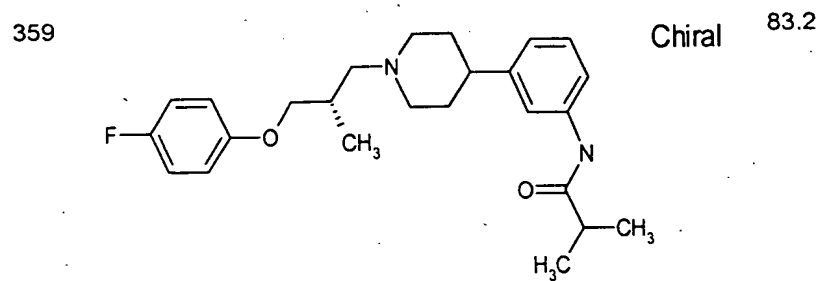
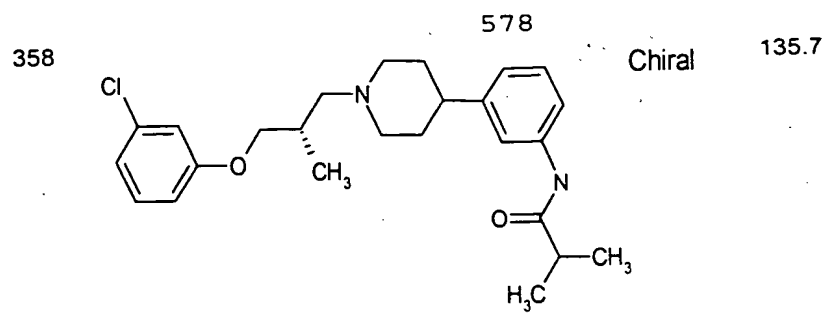


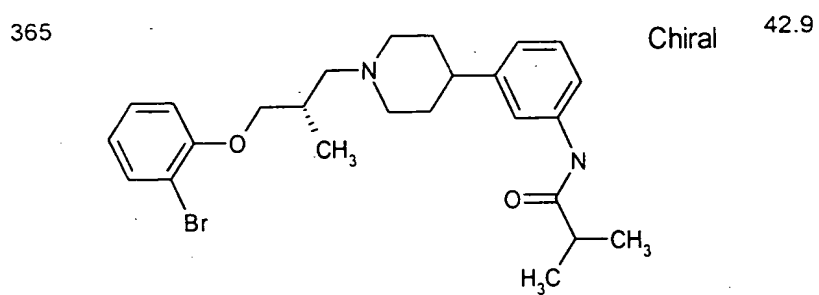
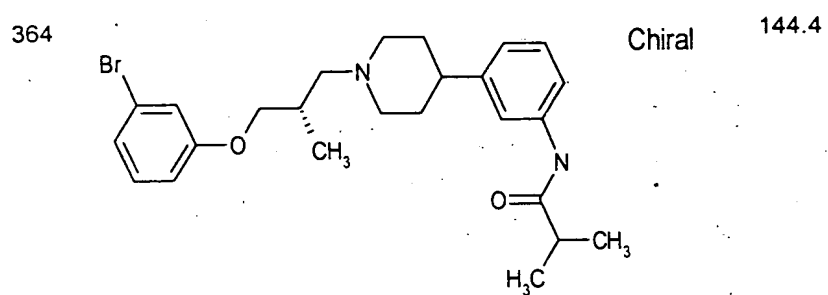
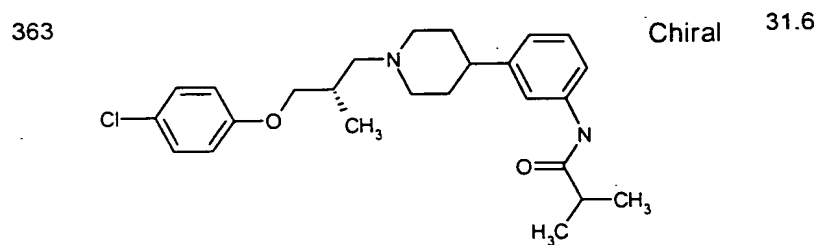
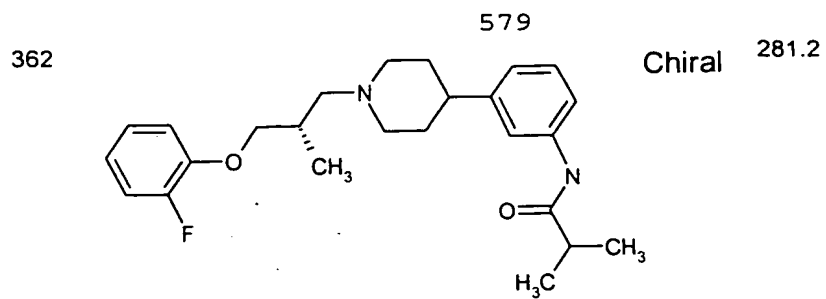
356 Chiral 54.5



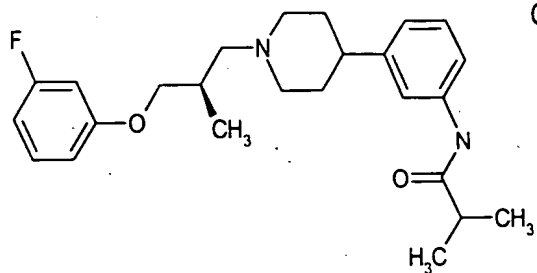
357 115.4



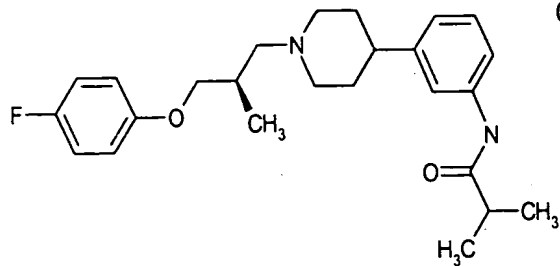




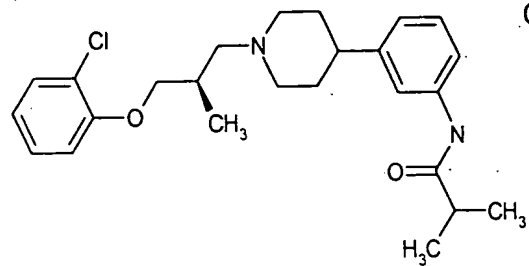
366 580 Chiral 645.5



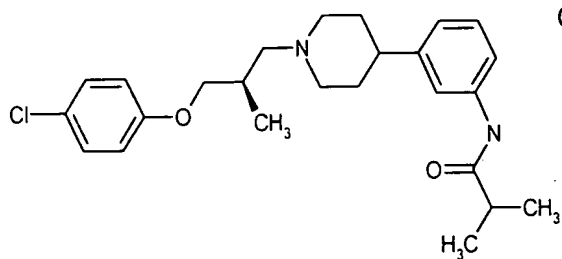
367 Chiral 235.7



368 Chiral 313.0



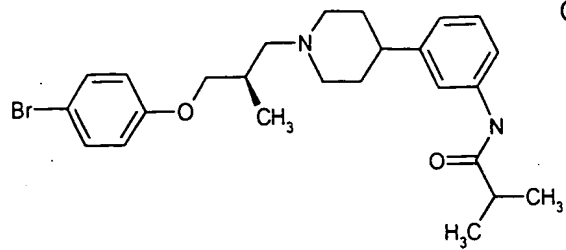
369 Chiral 145.0



370

581

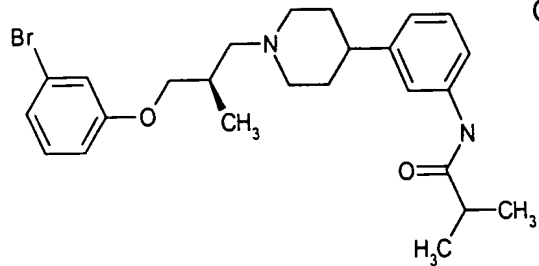
Chiral



371

Chiral

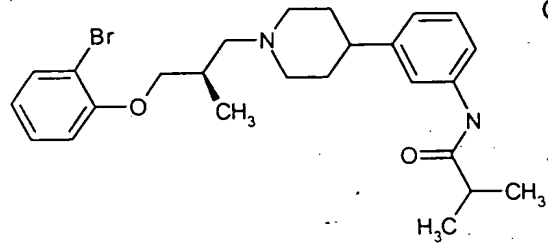
162.7



372

Chiral

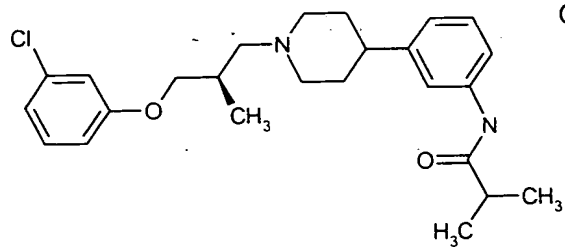
357.7

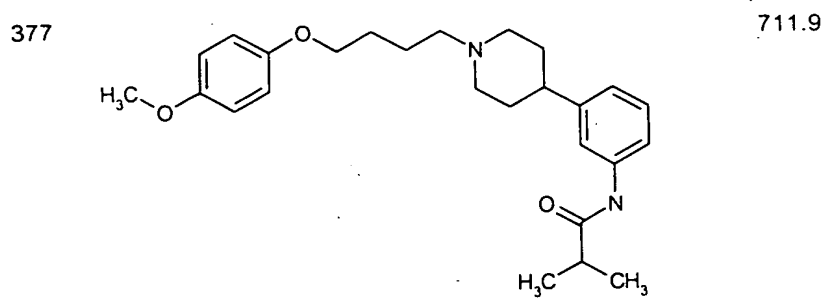
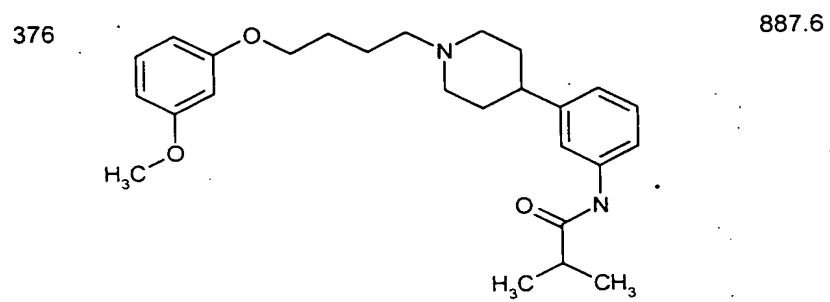
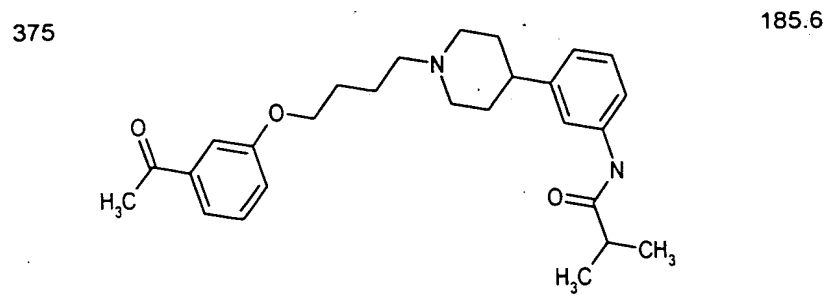
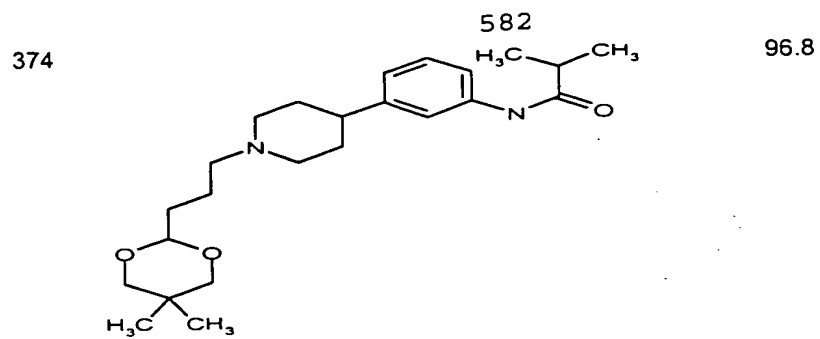


373

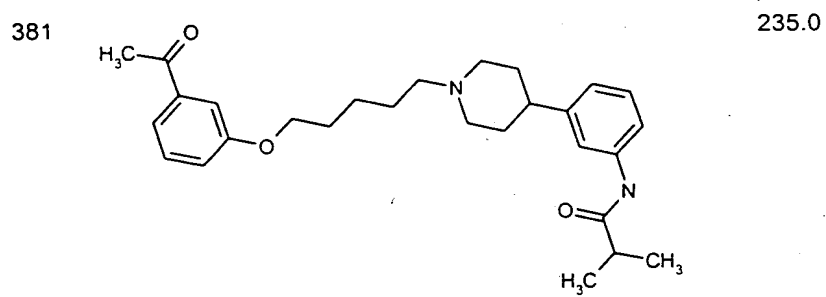
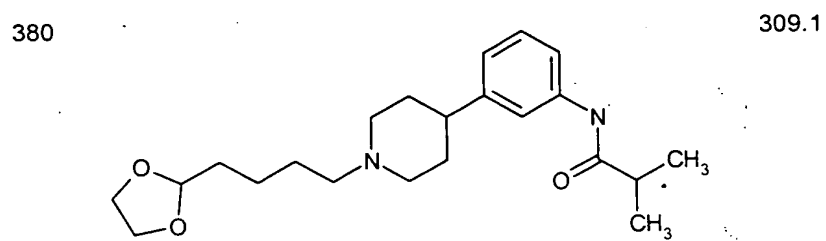
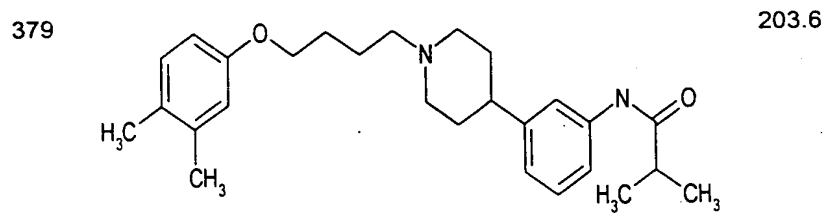
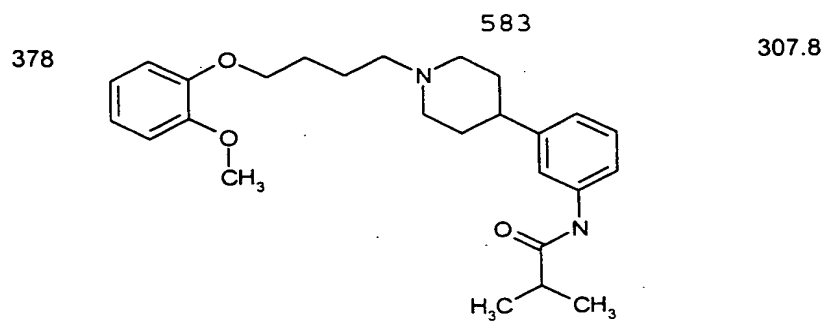
Chiral

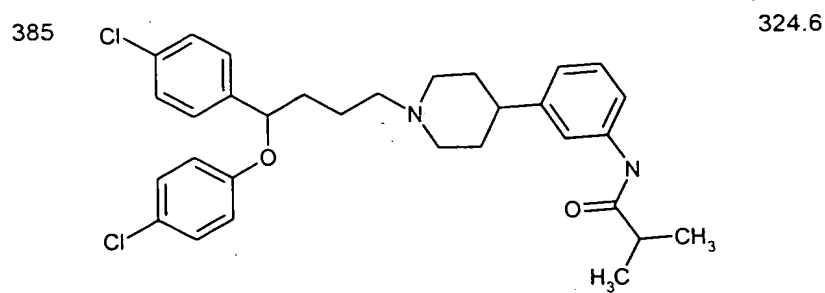
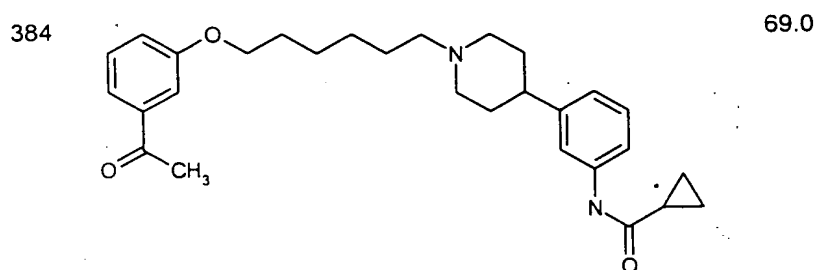
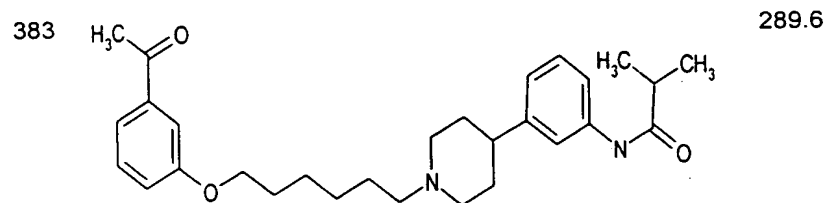
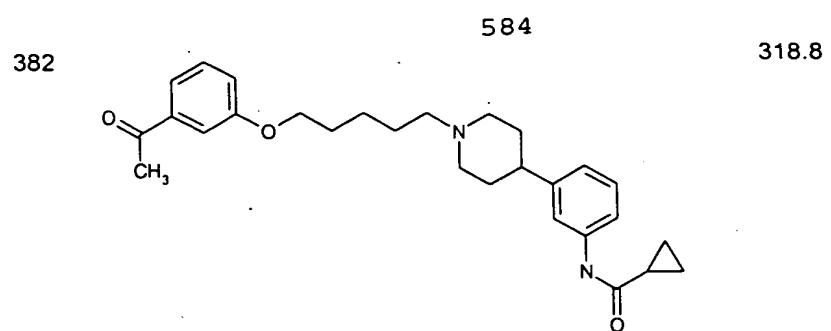
428.5











Example

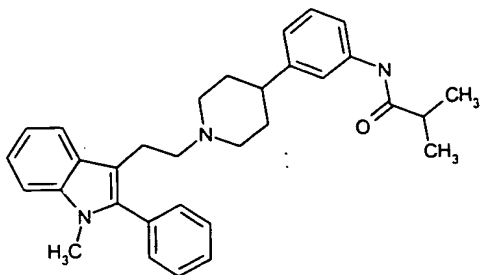
Structure

rMCH1  
Ki (nM)

386

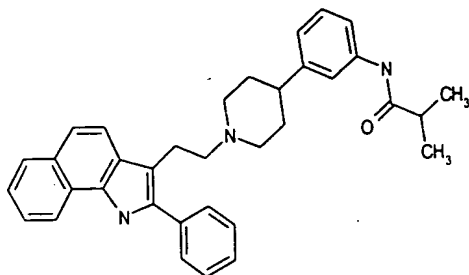
585

26.3



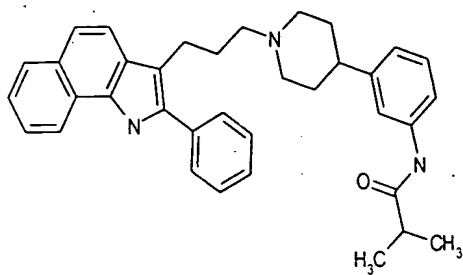
387

19.7



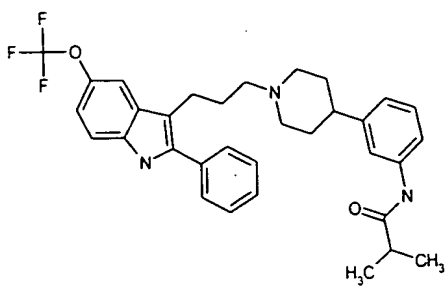
388

20.7

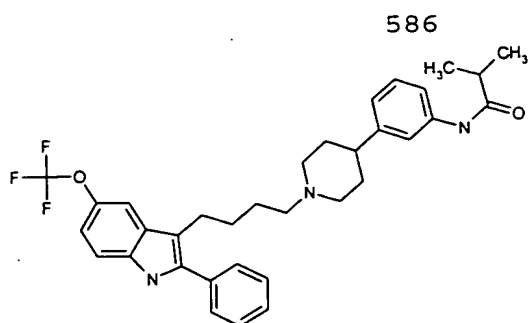


389

2.2

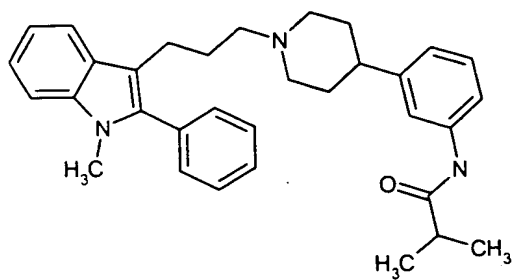


390



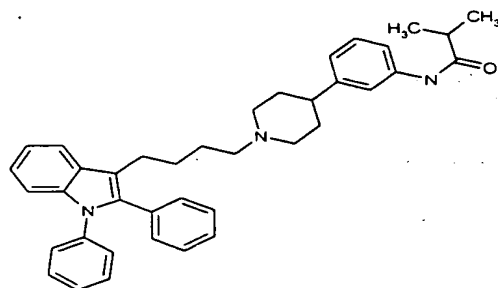
1.0

391



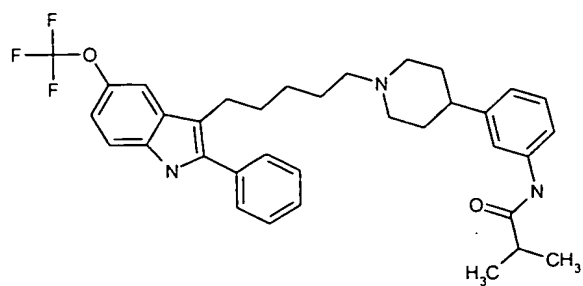
21.9

392



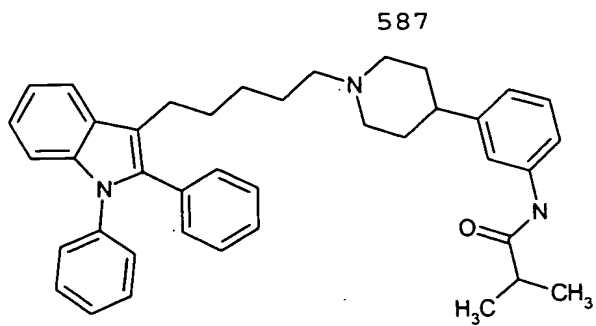
18.1

393

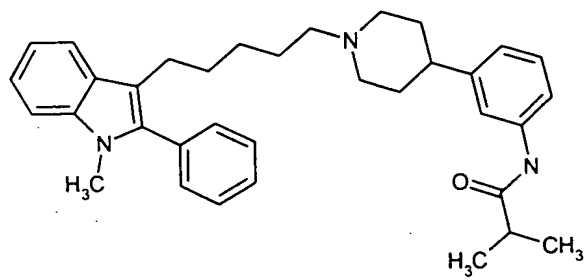


9.5

394

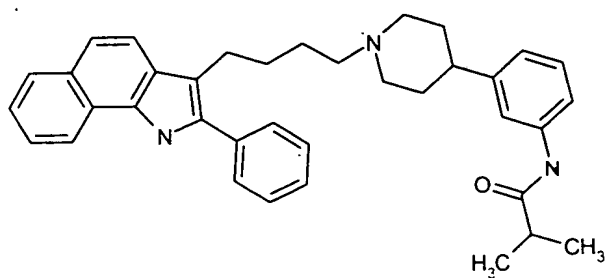


395

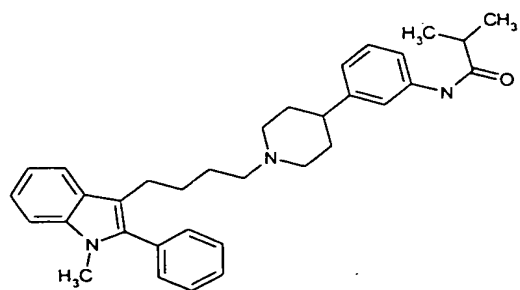


2.4

396



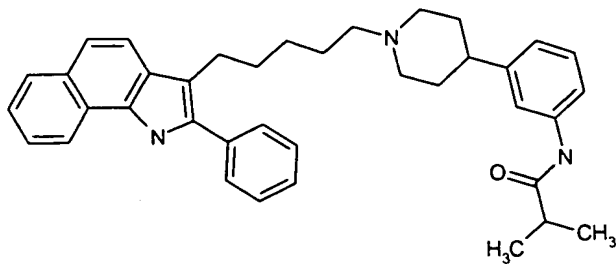
397



398

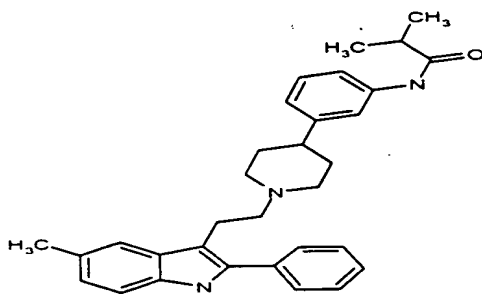
588

13.6



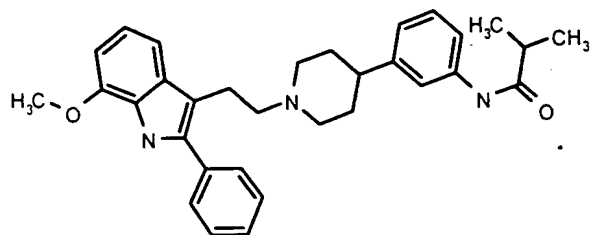
399

31.9



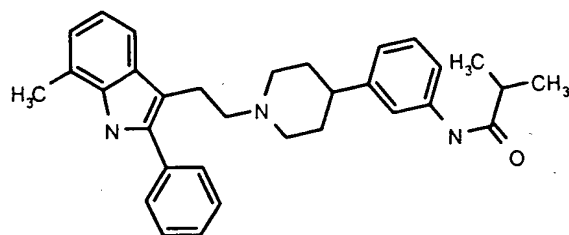
400

43.9



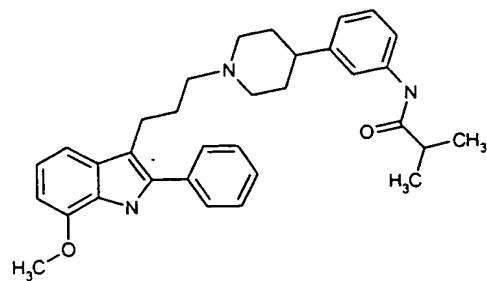
401

44.6



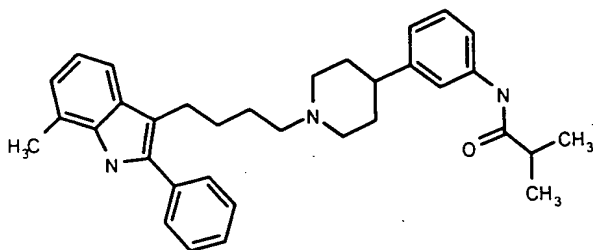
402

589

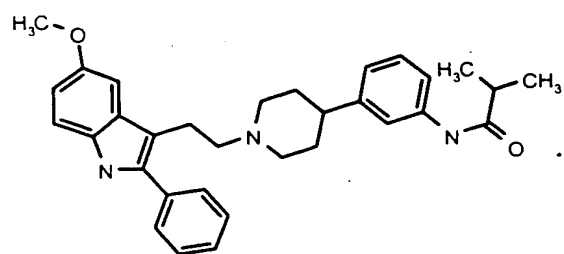


403

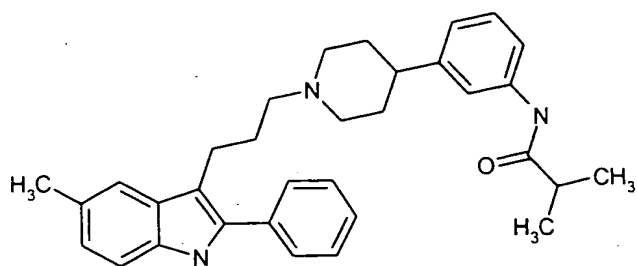
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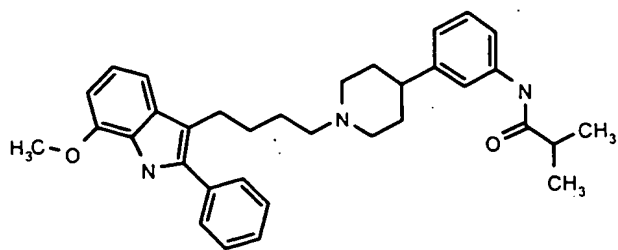
404



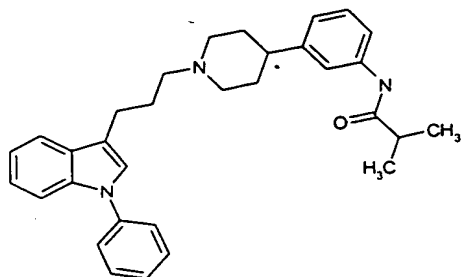
405



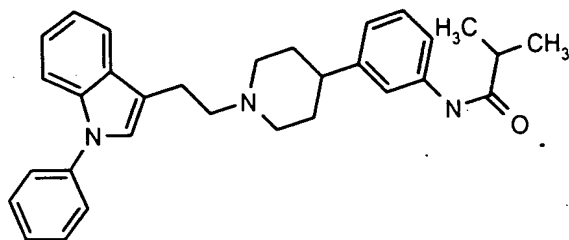
406 590 12.3



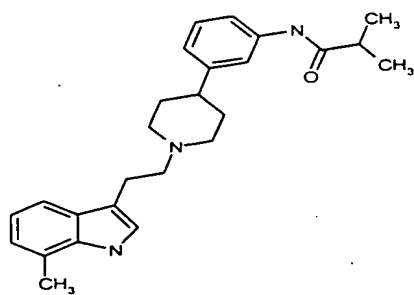
407 16.6



408 21.6

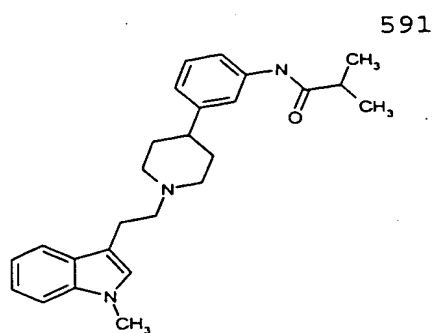


409 96.7



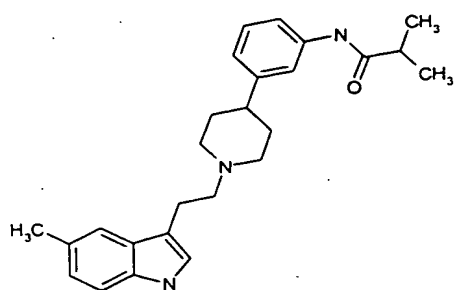


410



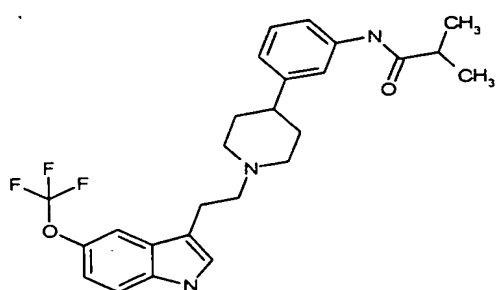
262.7

411



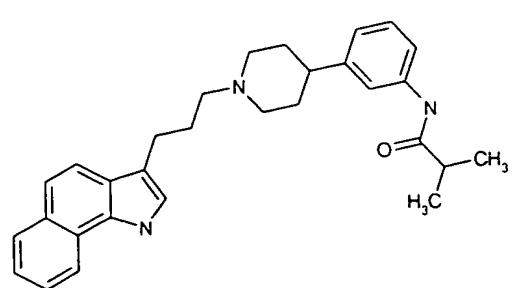
82.3

412



27.0

413

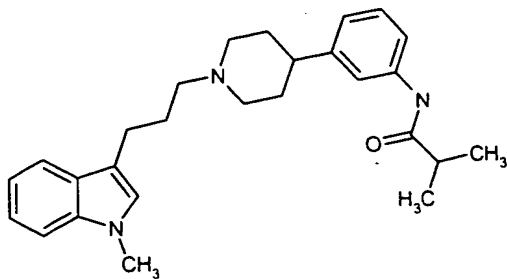


76.8

414

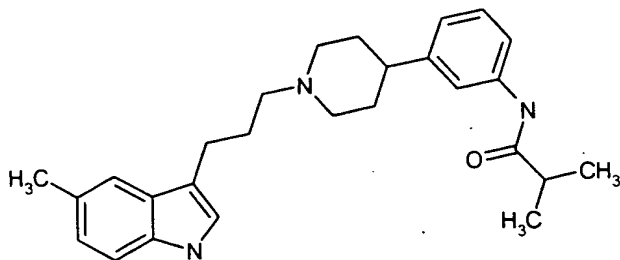
592

2.9



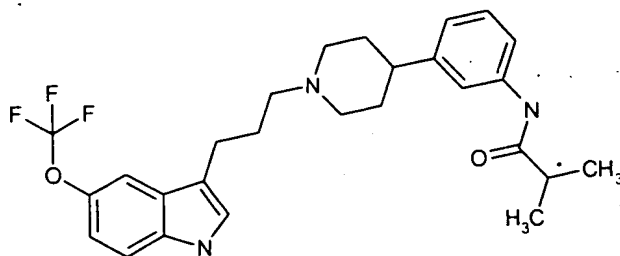
415

8.1



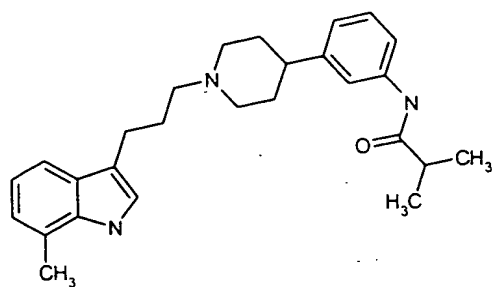
416

12.6



417

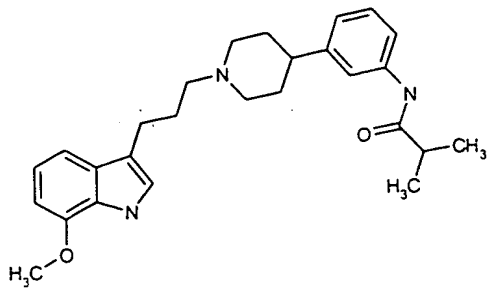
20.5



418

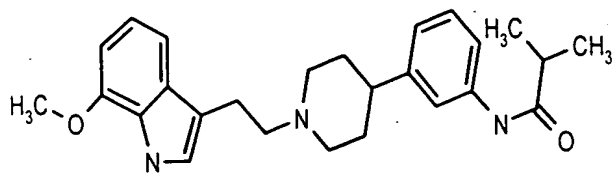
593

51.6

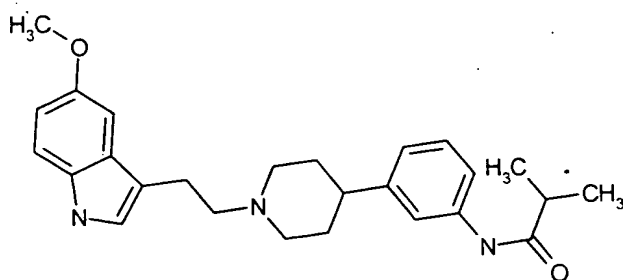


419

83.9

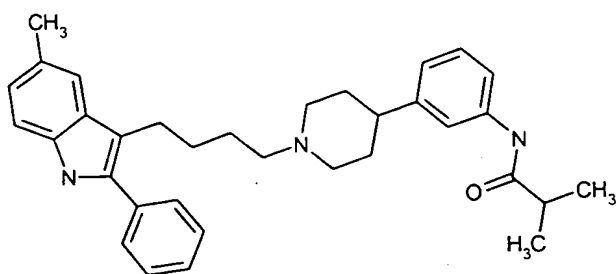


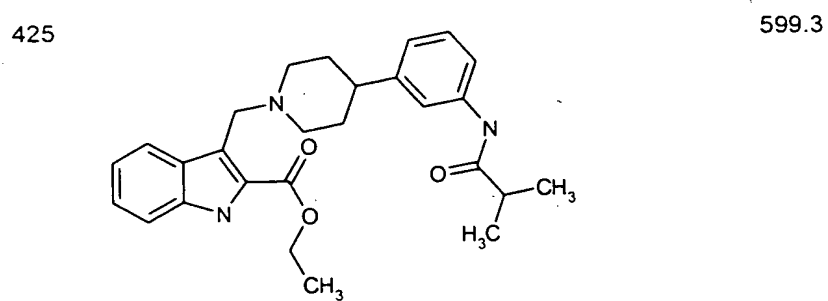
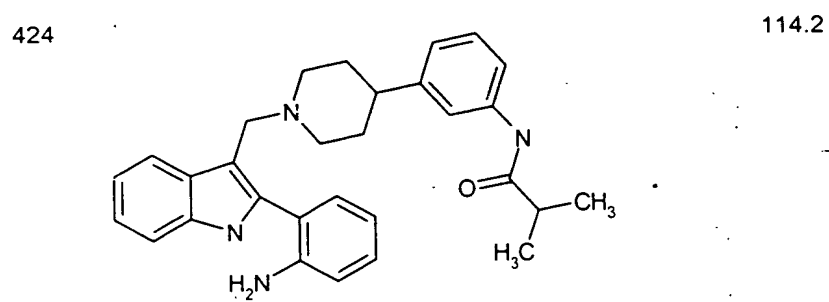
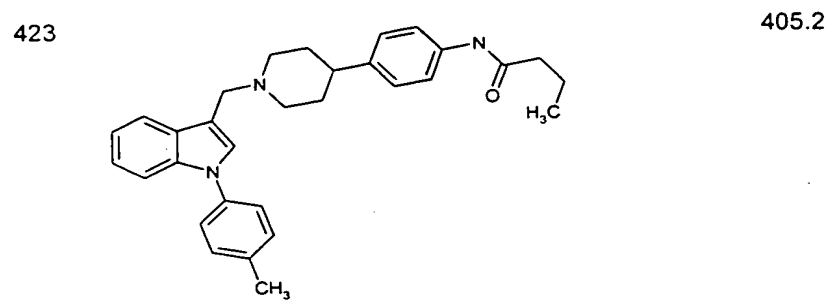
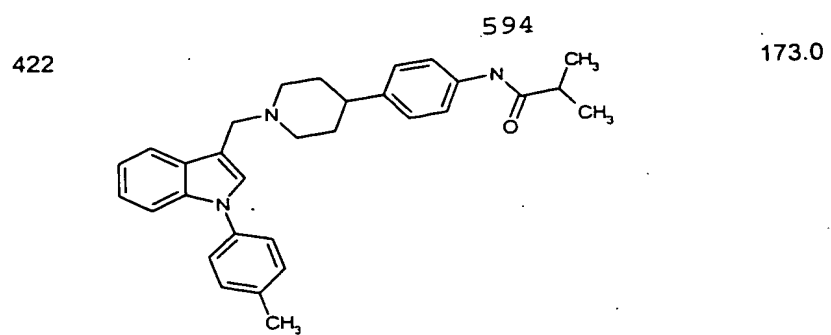
420



421

1.8

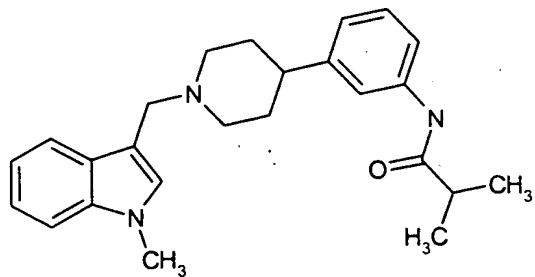




426

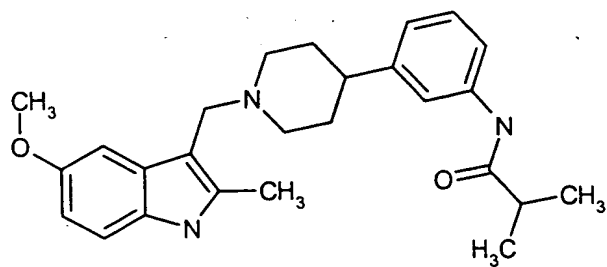
595

556.1



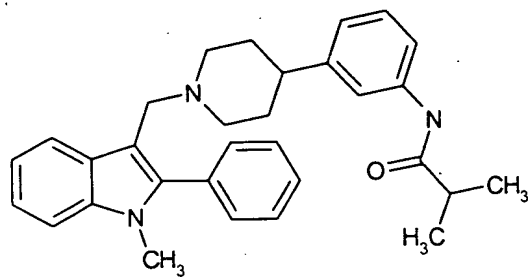
427

248.3



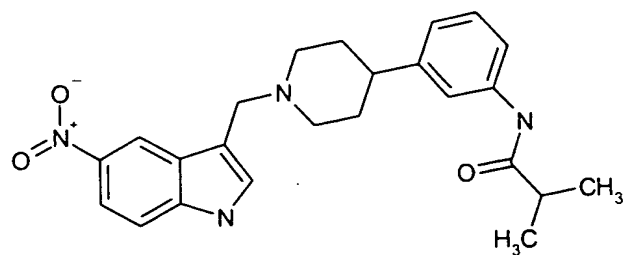
428

132.4



429

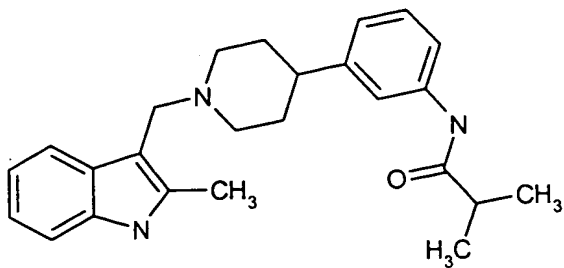
121.4



430

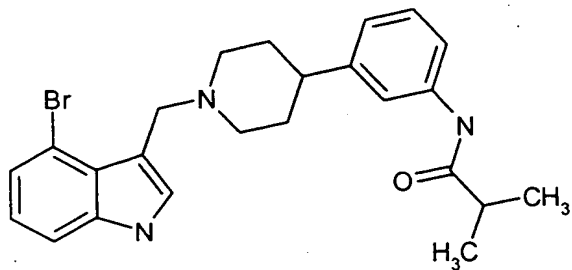
596

647.4



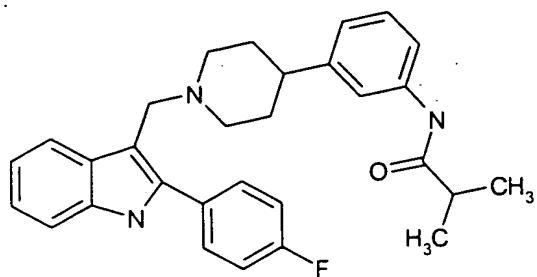
431

967.7



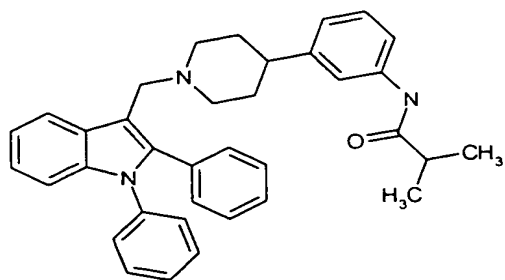
432

198.2



433

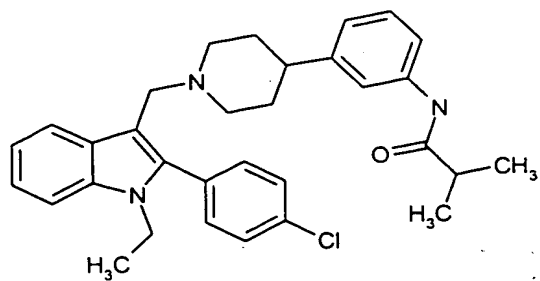
30.4



434

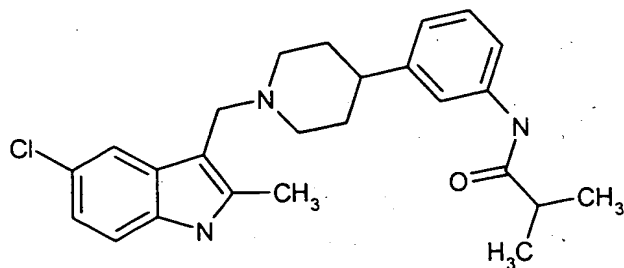
597

214.2



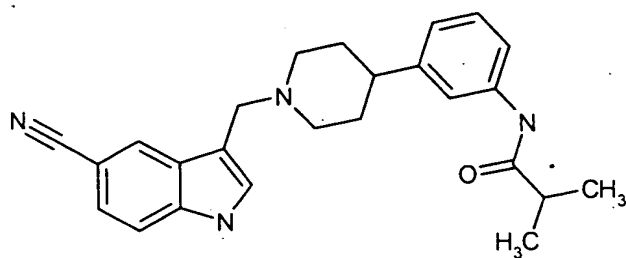
435

215.4



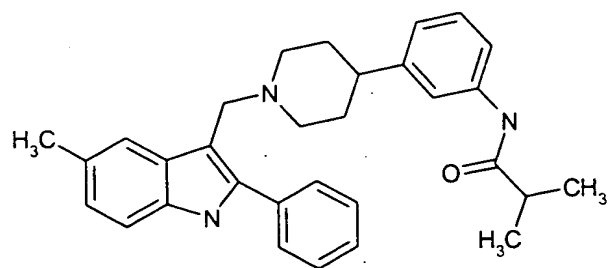
436

434.3



437

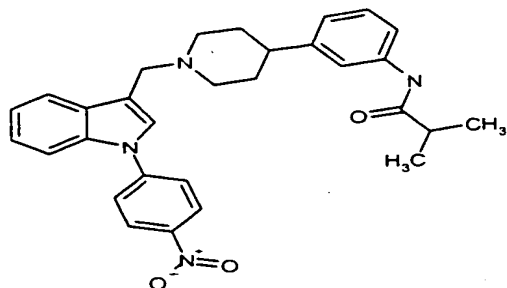
552.1



438

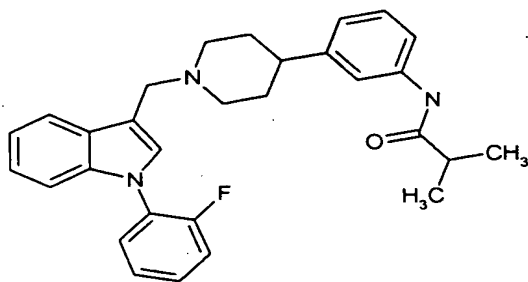
598

1.3



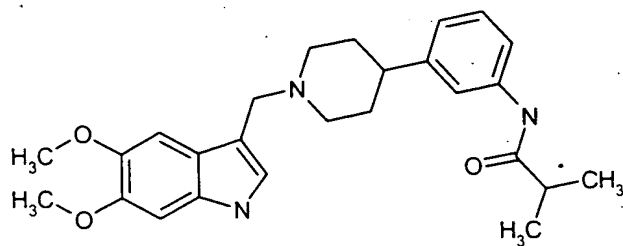
439

8.5



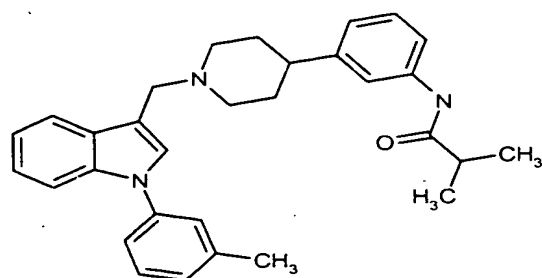
440

106.9



441

10.1

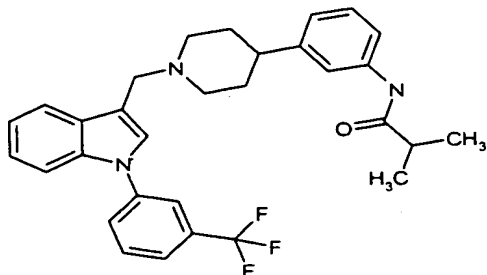




442

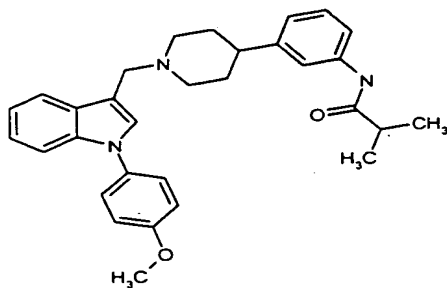
599

7.8



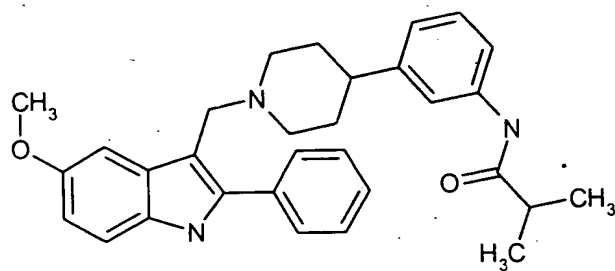
443

23.4



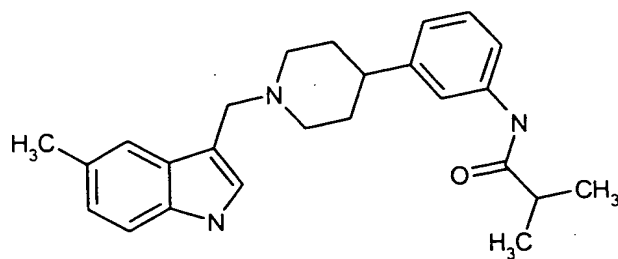
444

544.7



445

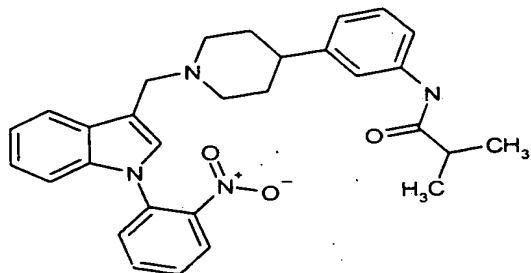
486.3



446

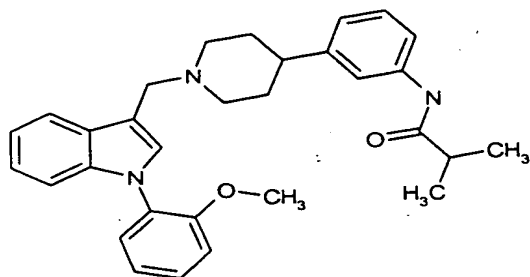
600

17.9



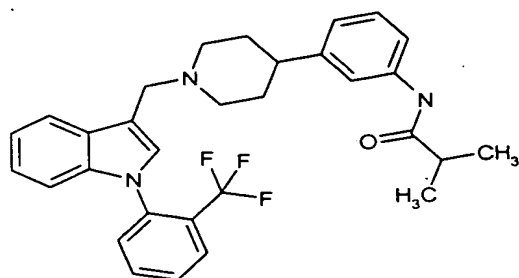
447

9.8



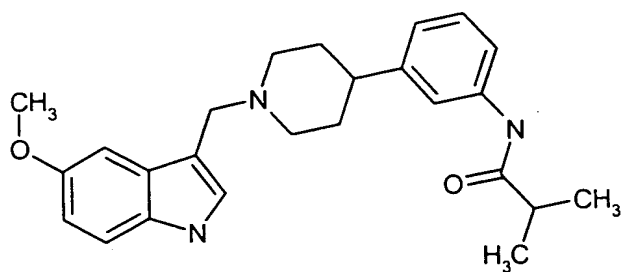
448

61.0



449

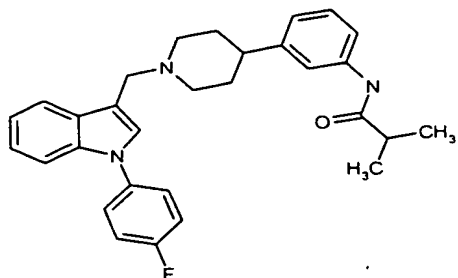
623.4



450

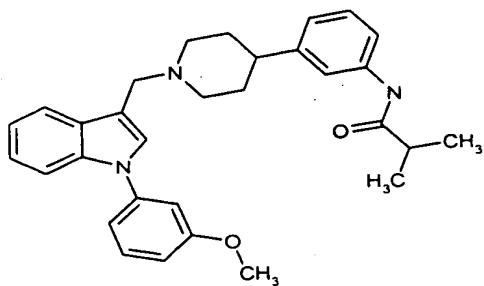
601

7.1



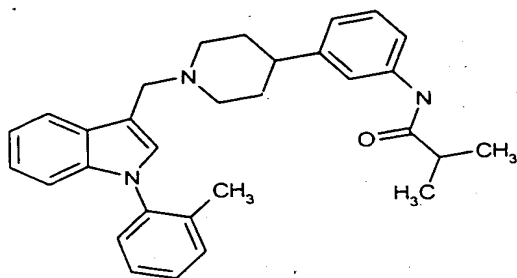
451

18.7



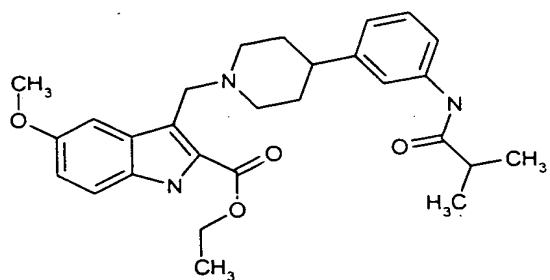
452

12.7



453

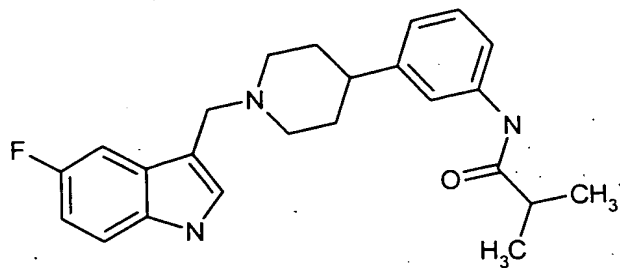
194.8



454

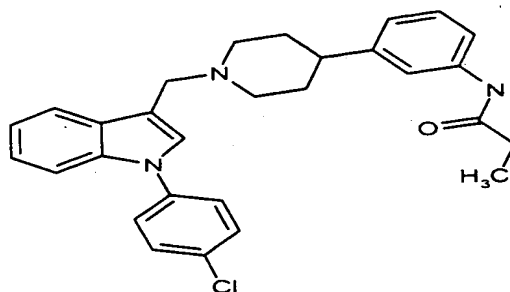
602

772.0



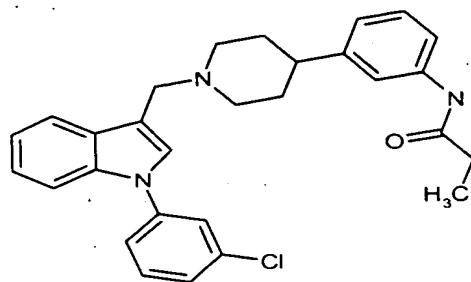
455

10.6



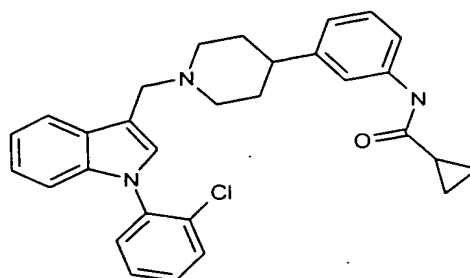
456

28.0



457

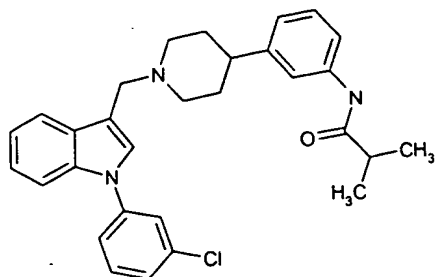
27.4



458

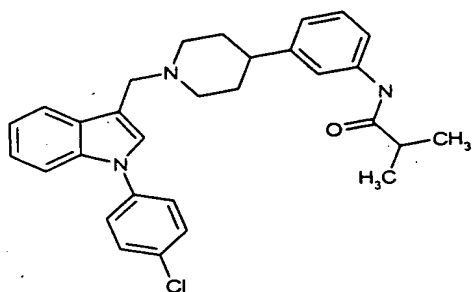
603

15.3



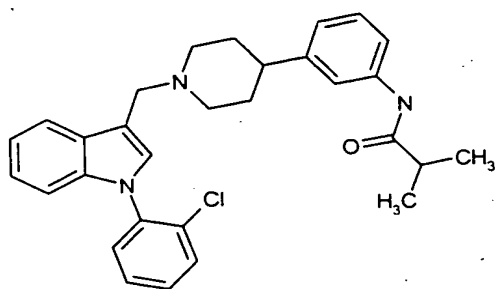
459

10.4



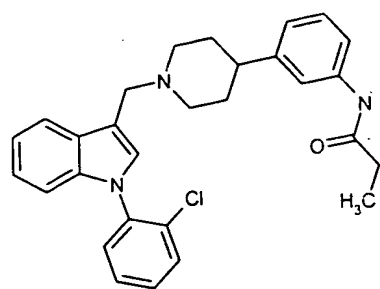
460

9.1



461

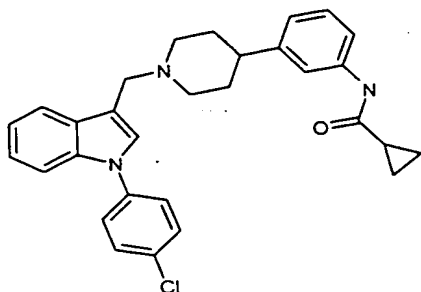
35.6



462

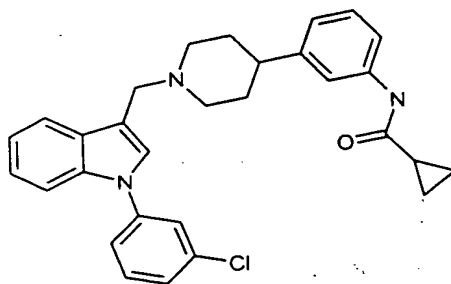
604

12.4



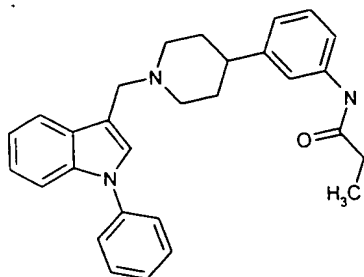
463

17.2



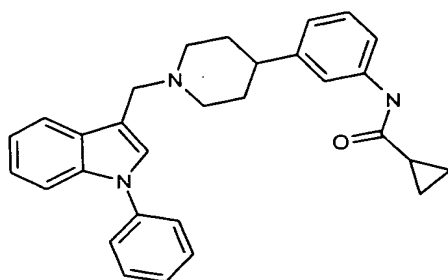
464

84.1

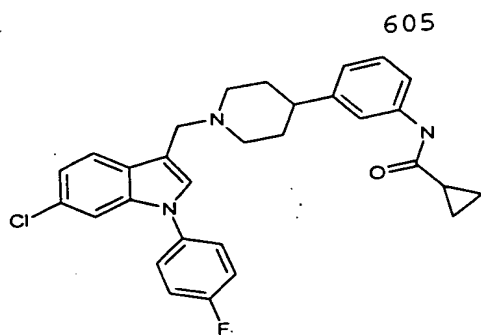


465

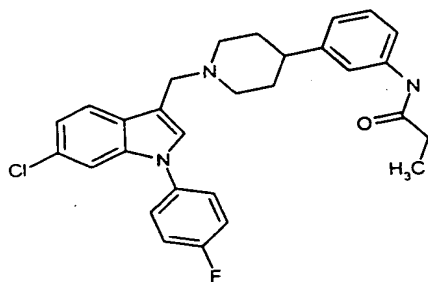
10.7



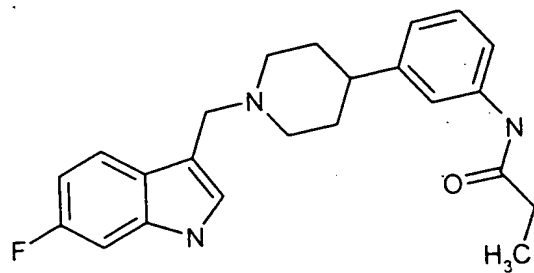
466



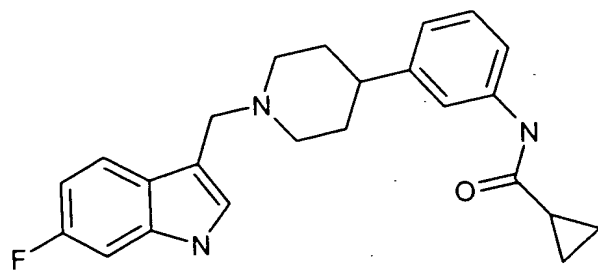
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468



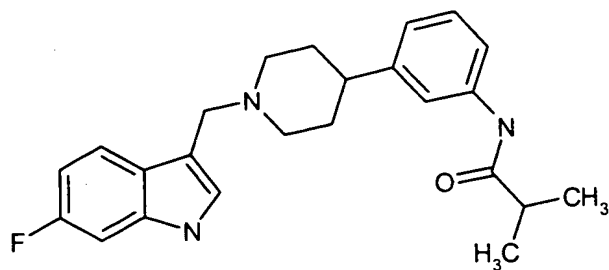
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470

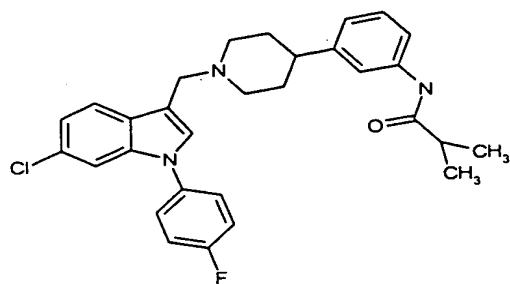
606

654.1



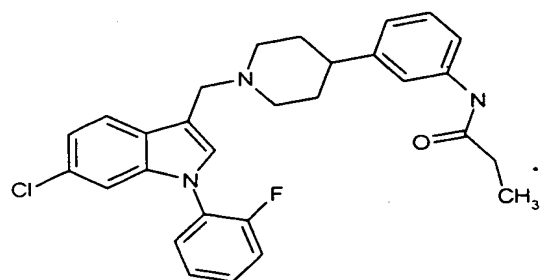
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4.3



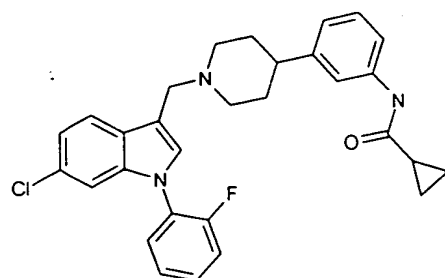
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12.2



473

11.3

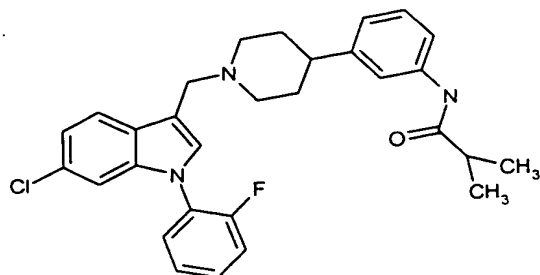




474

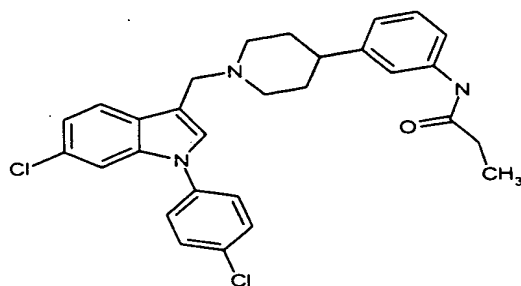
607

13.3



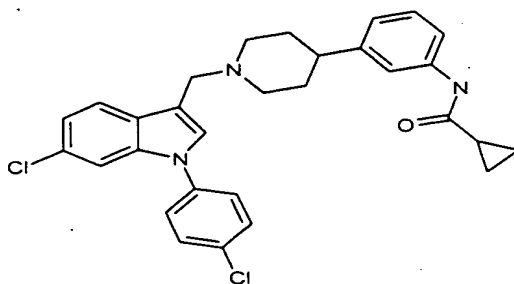
475

12.4



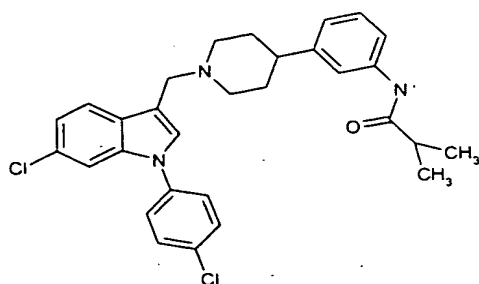
476

12.7



477

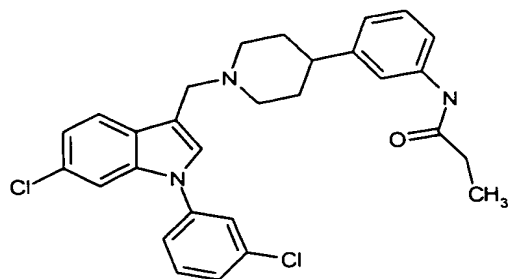
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478

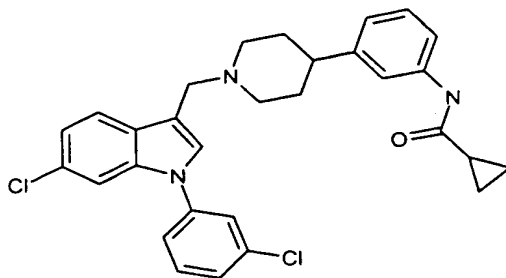
608

11.7



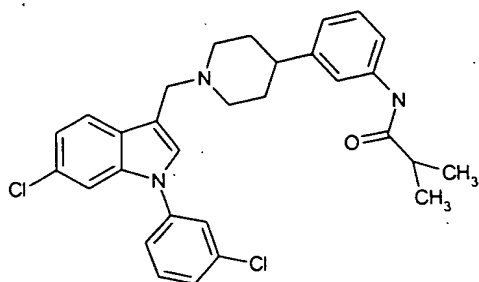
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8.1



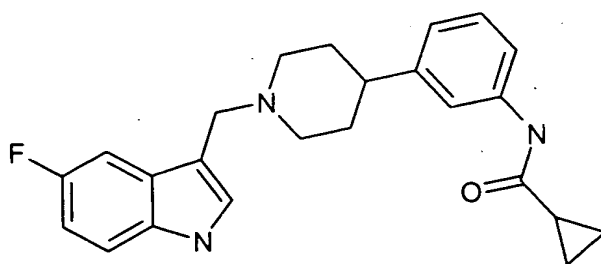
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9.0



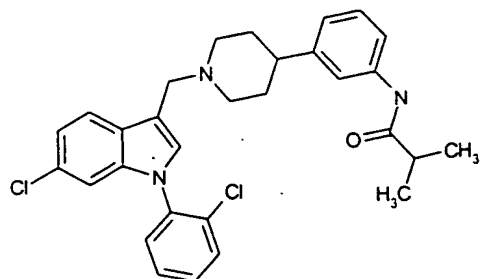
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664.0

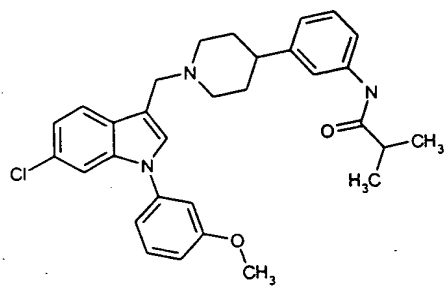


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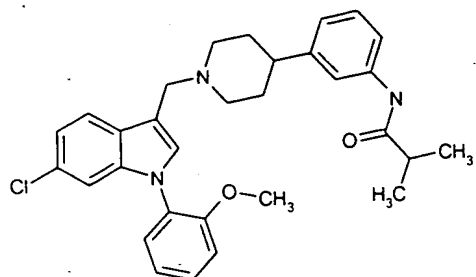
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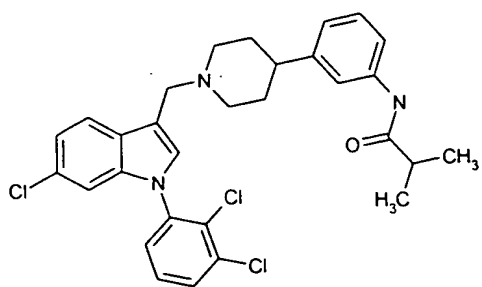
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484

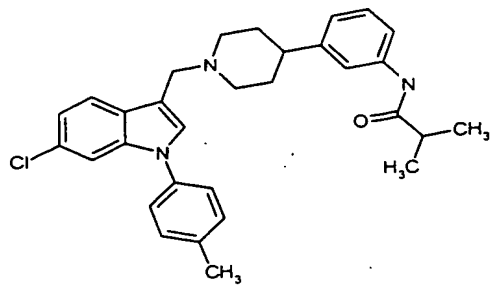


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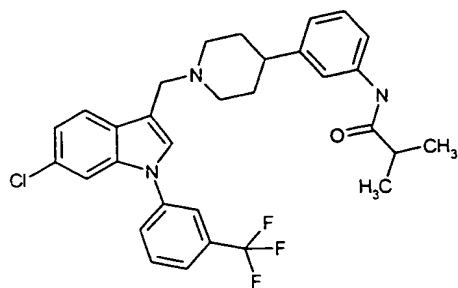


610

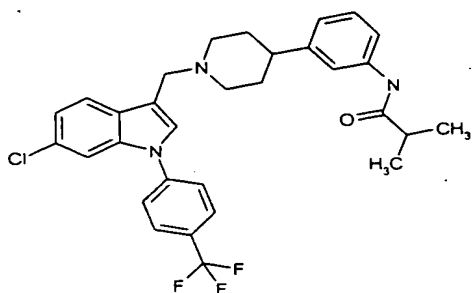
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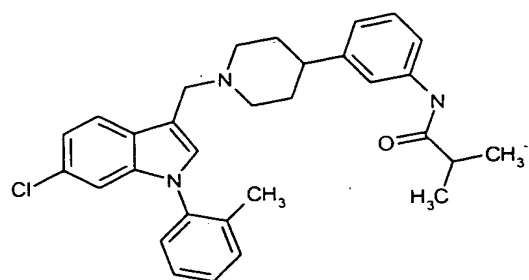
487



488

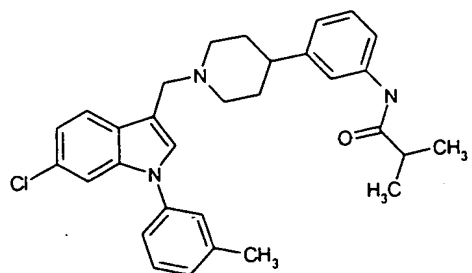


489

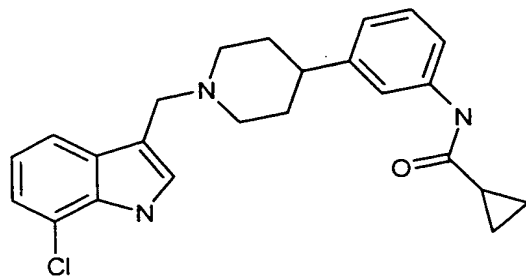


611

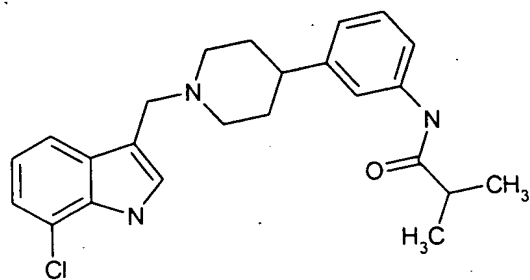
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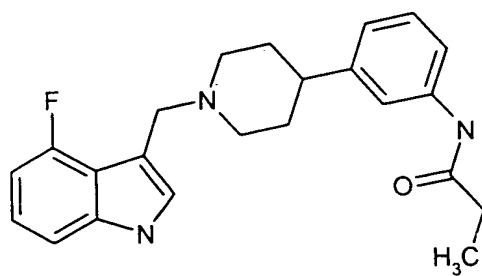
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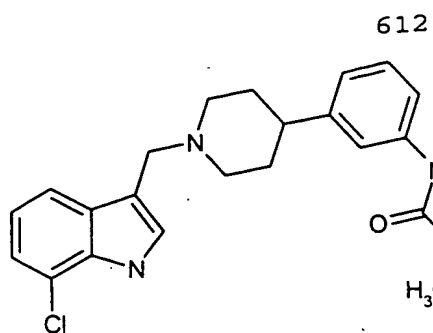
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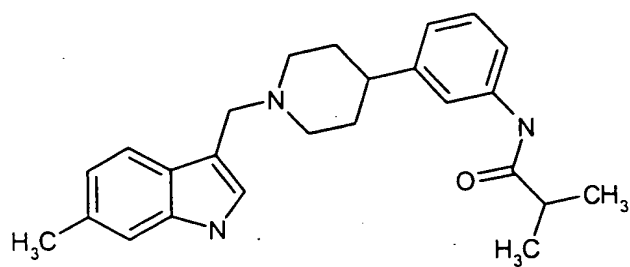
493



494

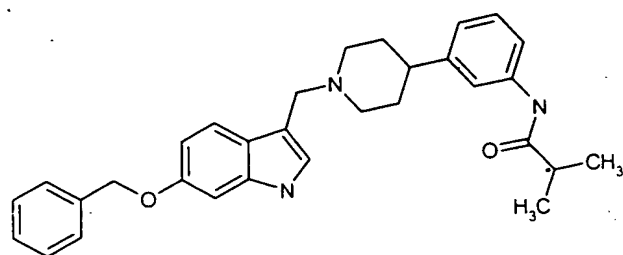


495



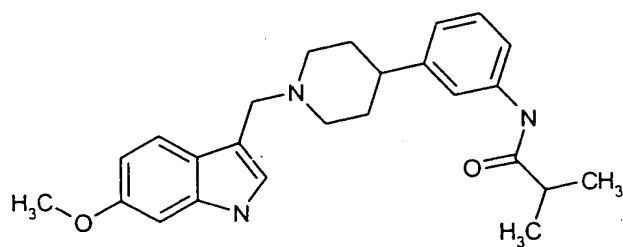
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496



288.0

497

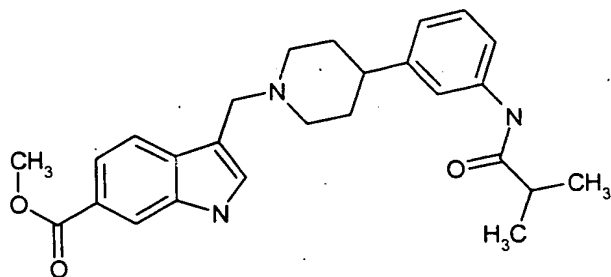


97.7

498

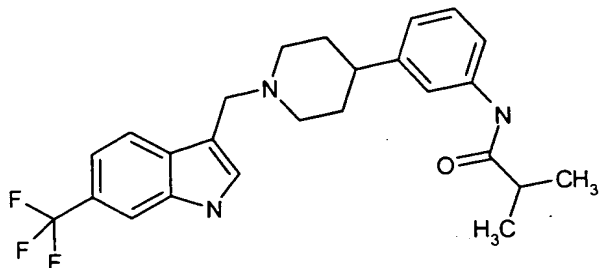
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52.2



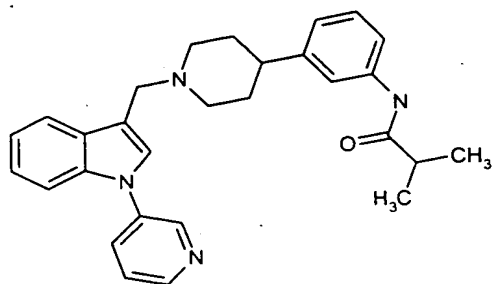
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11.9



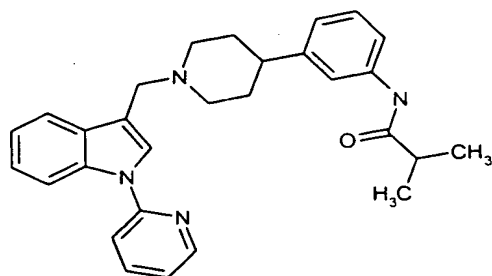
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29.4



501

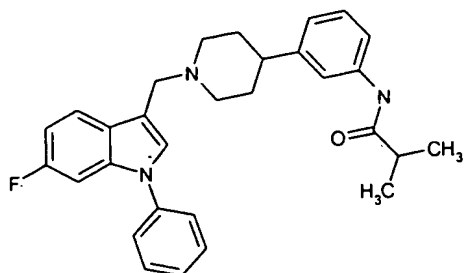
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502

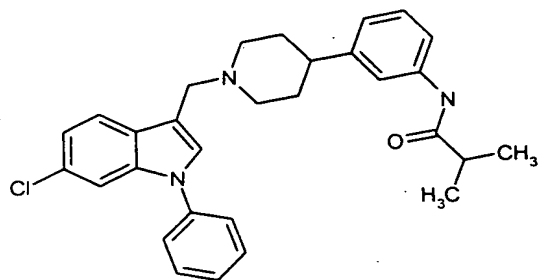
614

## 4.6



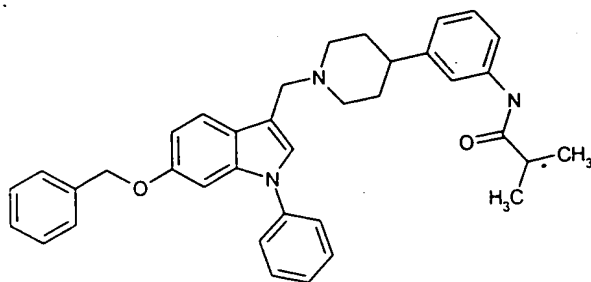
503

## 6.0



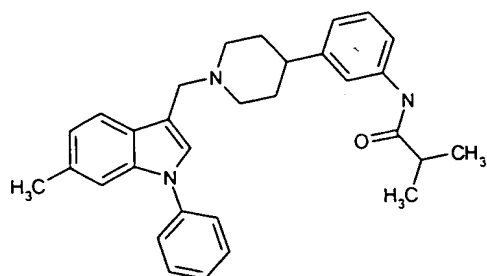
504

22.5



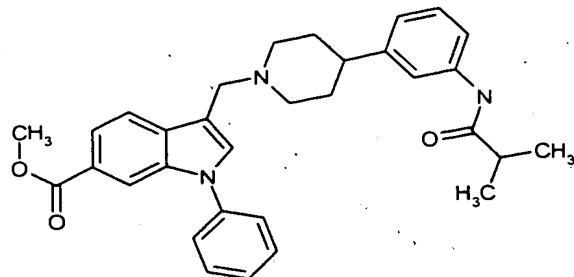
505

## 6.5

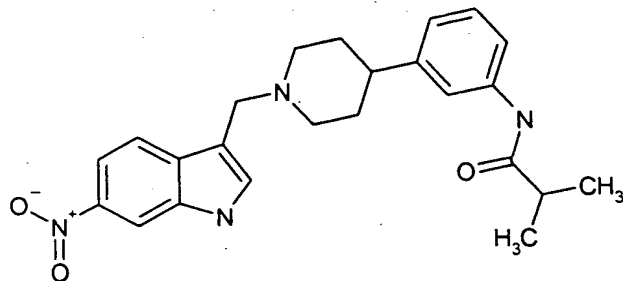




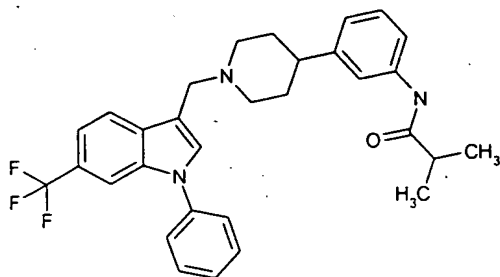
506 615 2.5



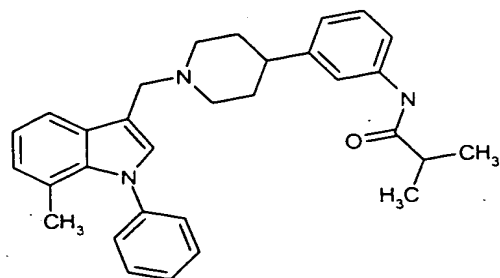
507 57.9



508 8.5



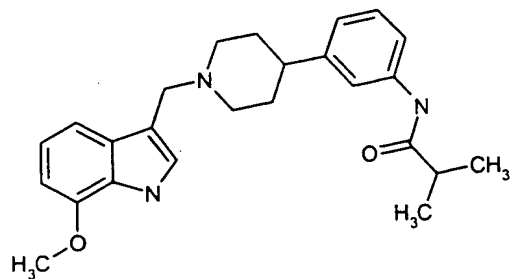
509 24.3



510

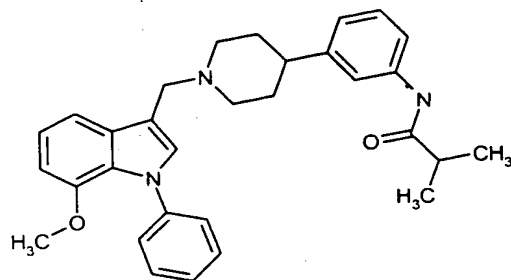
616

304.9



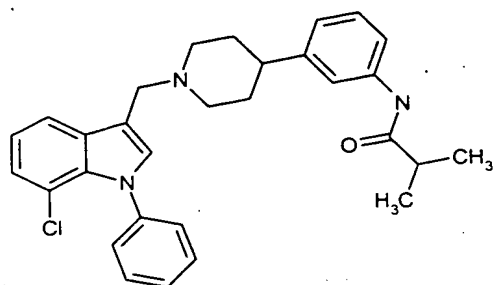
511

6.0



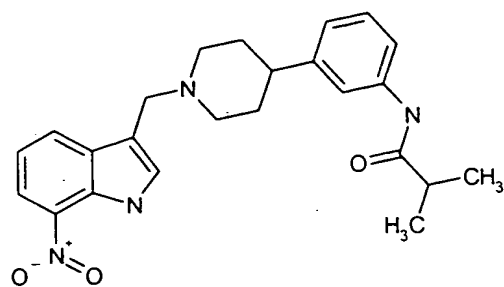
512

42.7



513

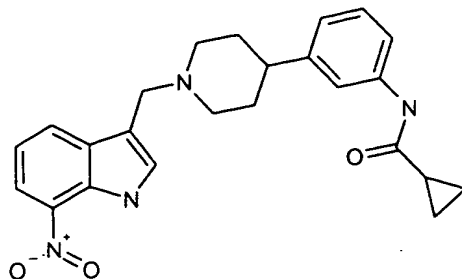
178.7



514

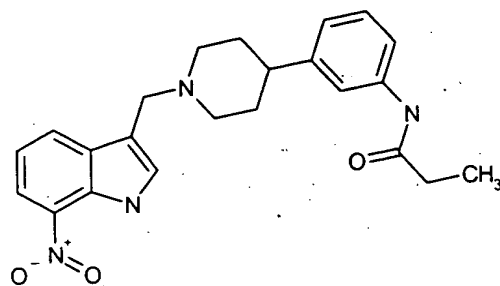
617

151.4



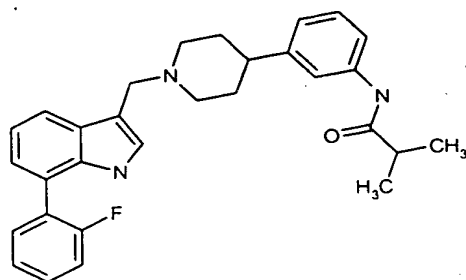
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296.2



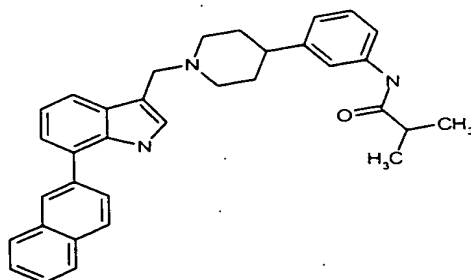
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90.9

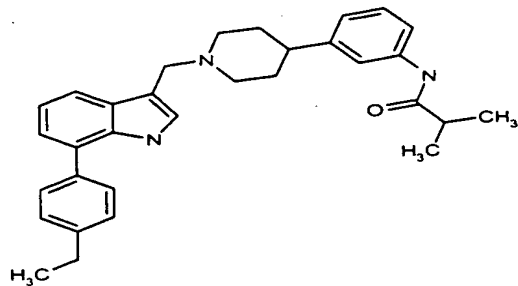


517

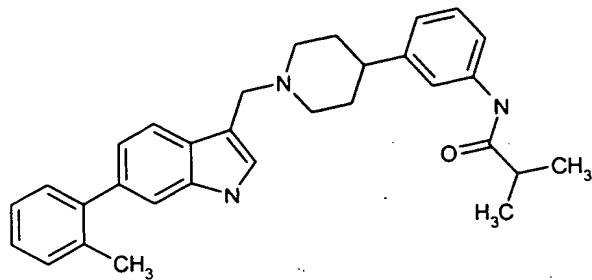
286.9



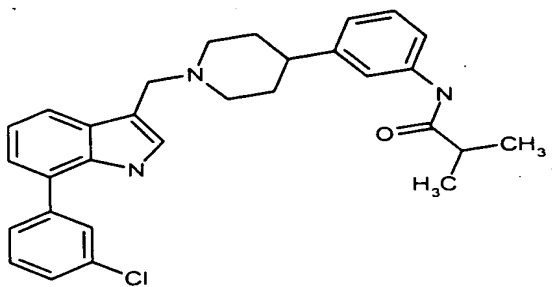
518 618 226.2



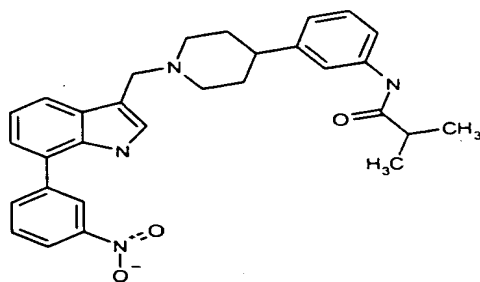
519 80.9



520 135.1



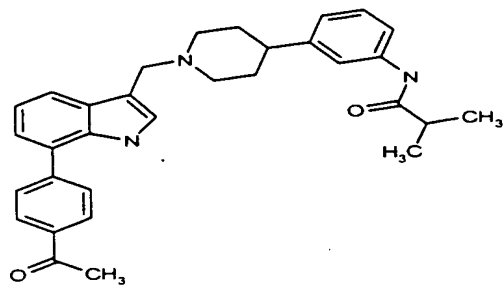
521 27.0



522

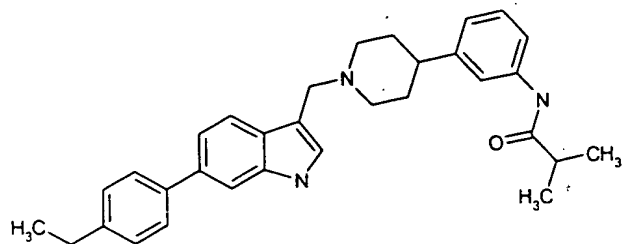
619

247.0



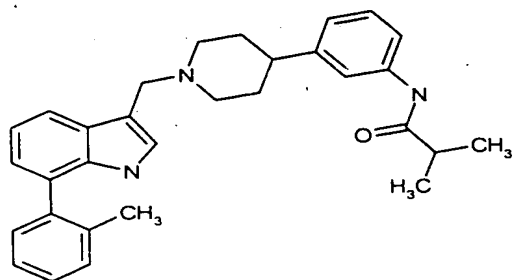
523

54.8



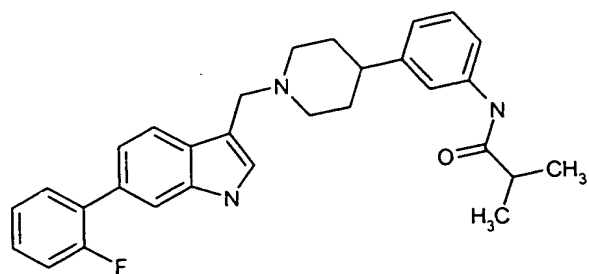
524

198.7



525

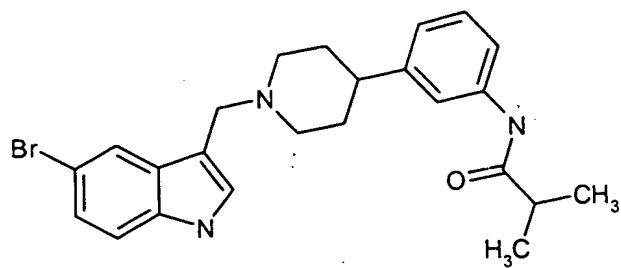
91.4



526

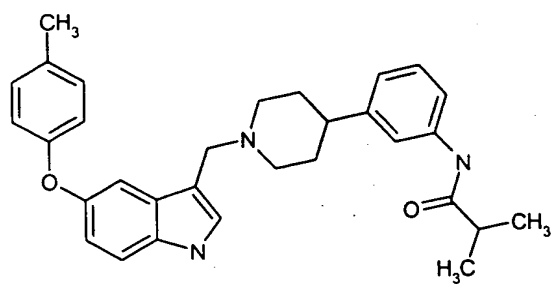
620

410.6



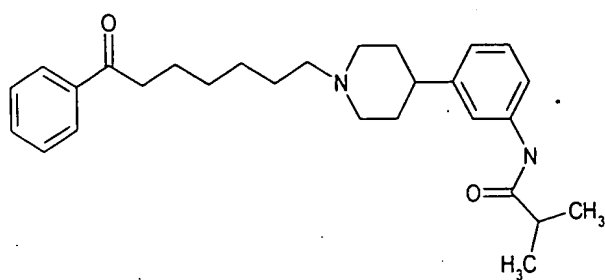
527

226.5



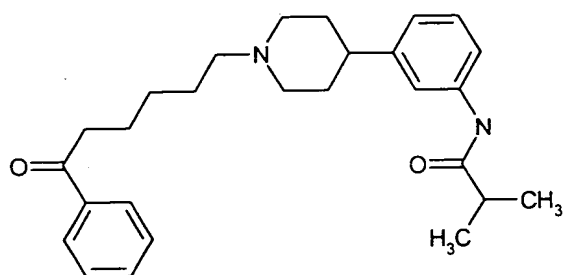
528

115.1



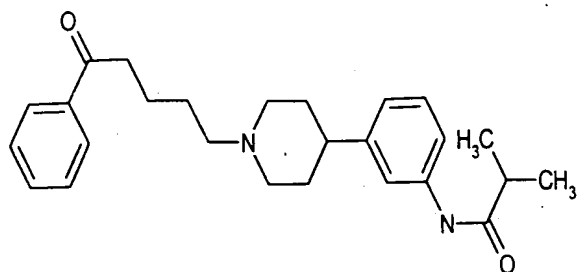
529

42.4



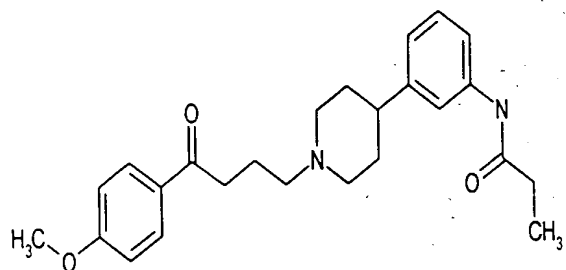
621

530



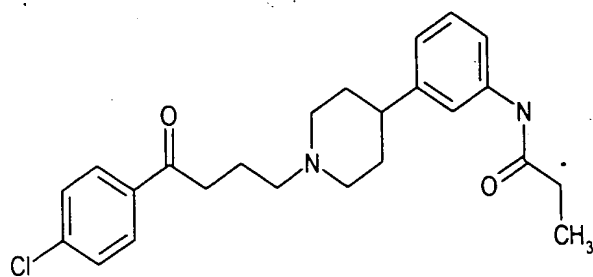
531

105.3



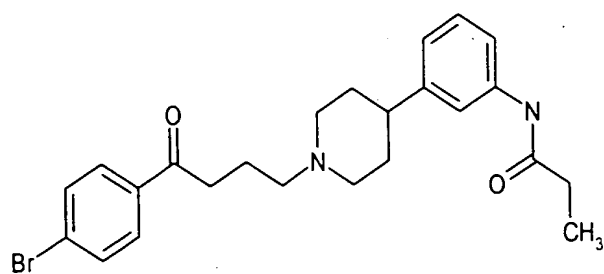
532

8.7



533

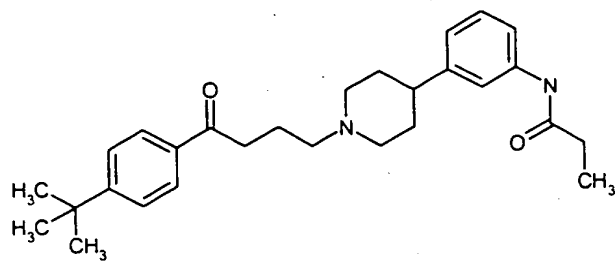
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534

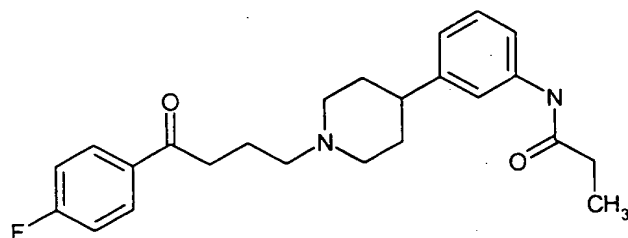
622

154.9



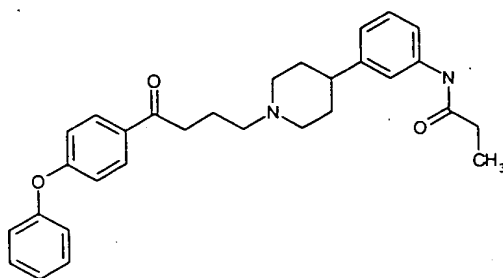
535

28.1



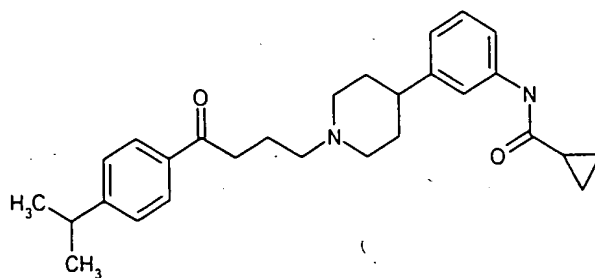
536

150.4



537

67.7

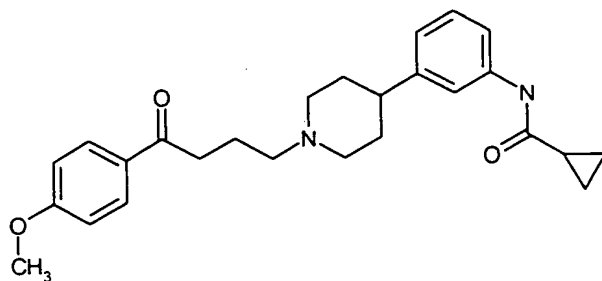




538

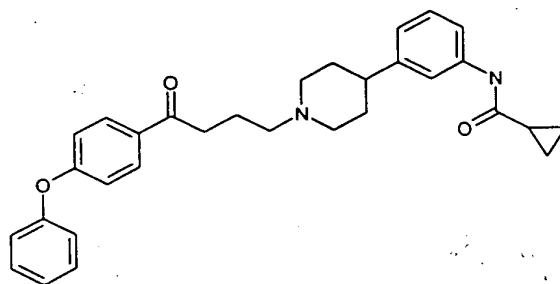
623

36.3



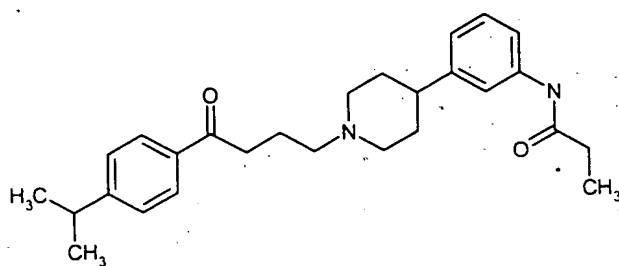
539

268.4



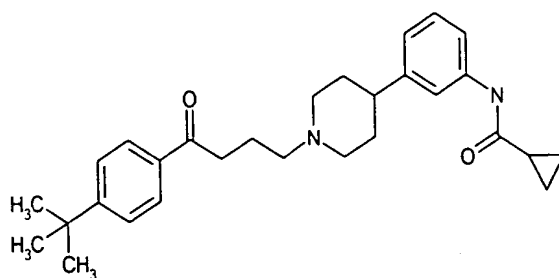
540

172.3



541

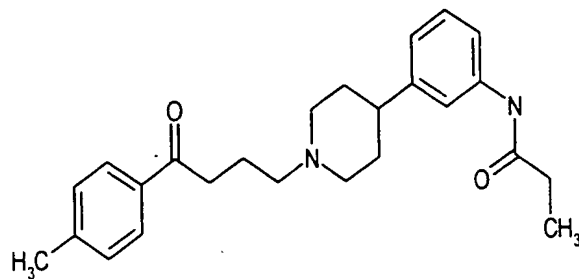
318.6



542

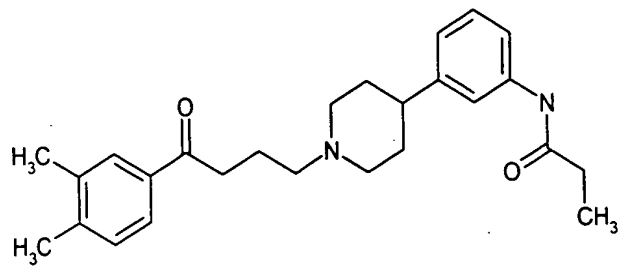
624

31.3



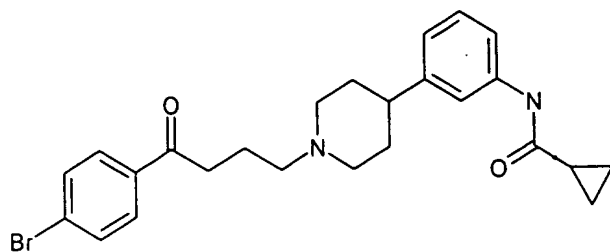
543

27.6



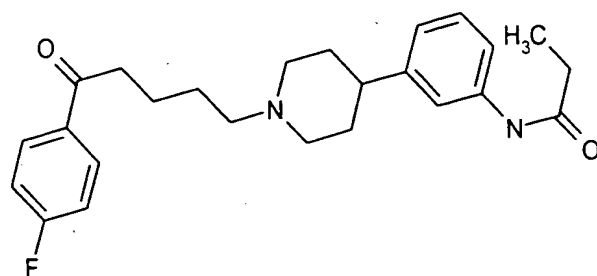
544

16.2



545

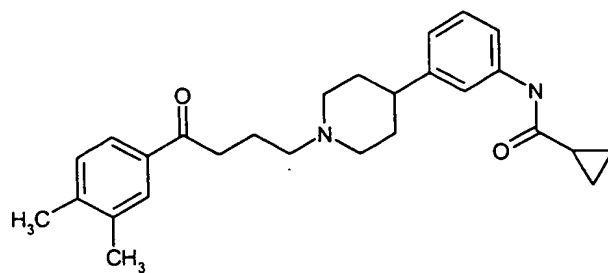
52.0



546

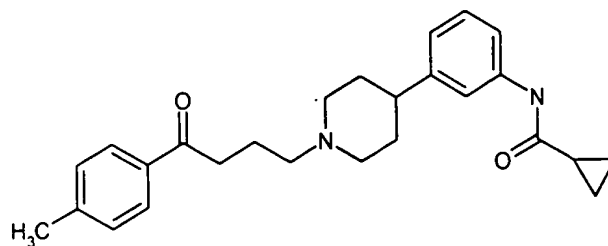
625

87.9



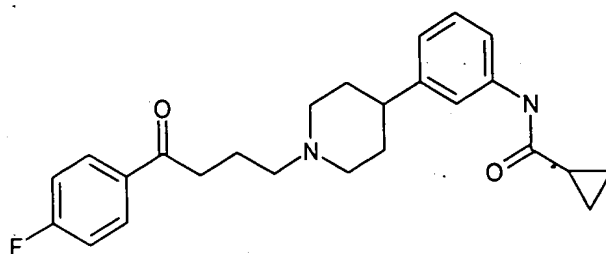
547

75.5



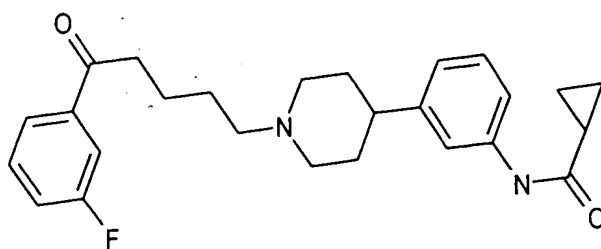
548

125.6

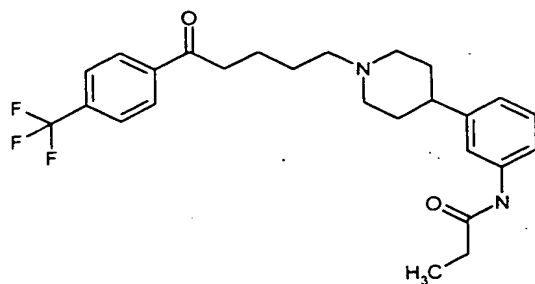


549

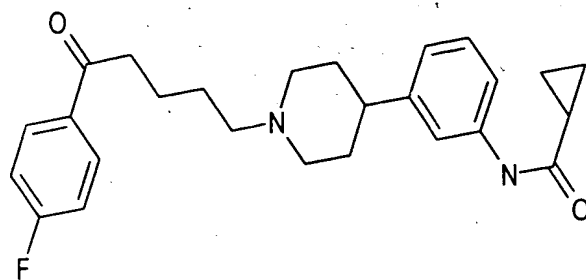
39.7



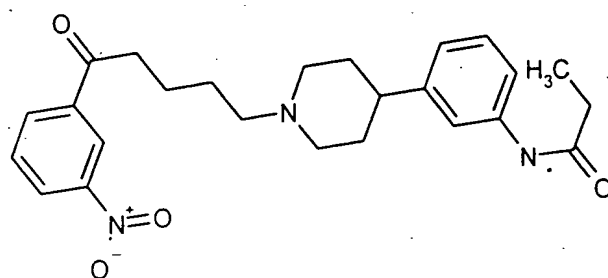
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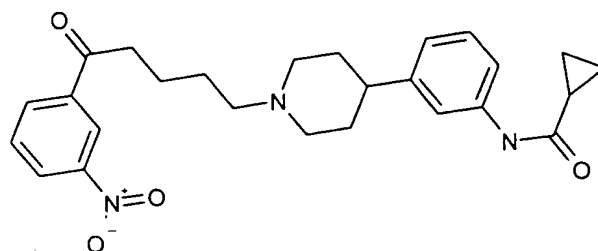
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552 24.7



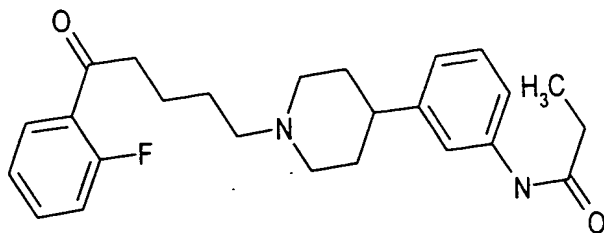
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627

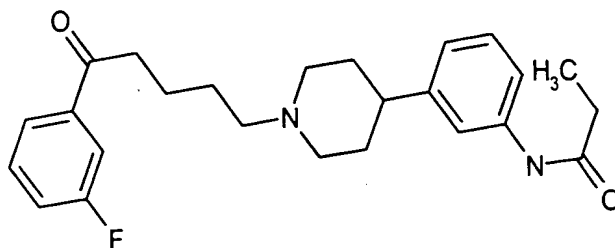
554

70.9



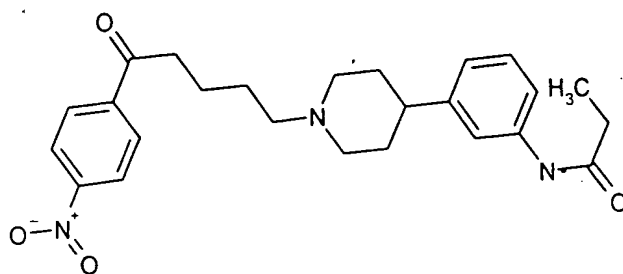
555

50.3



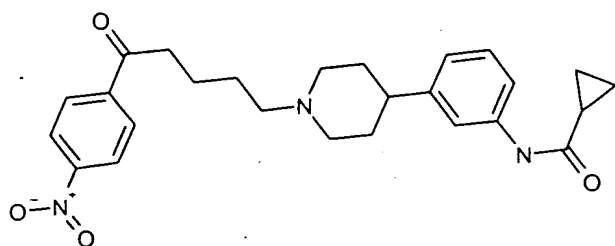
556

35.6

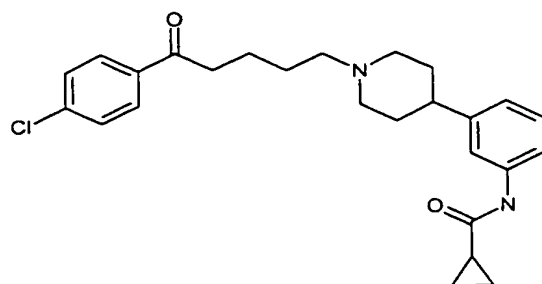


557

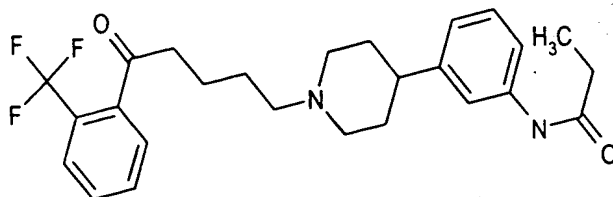
25.6



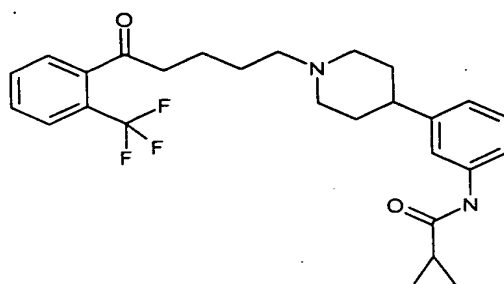
558 628 20.2



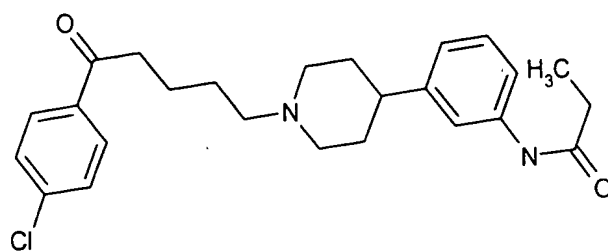
559 62.3



560 55.7



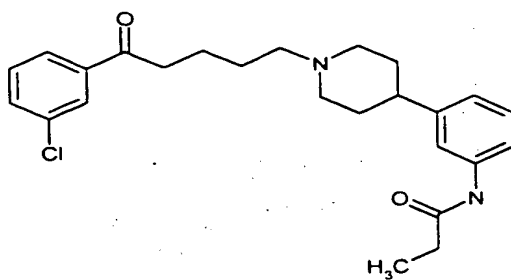
561 92.9



562

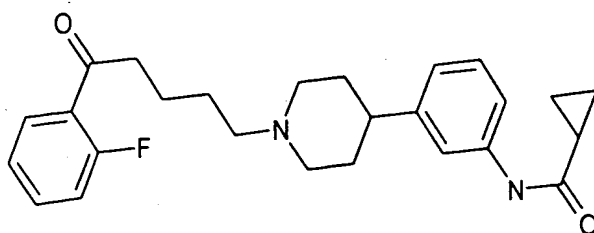
629

48.1



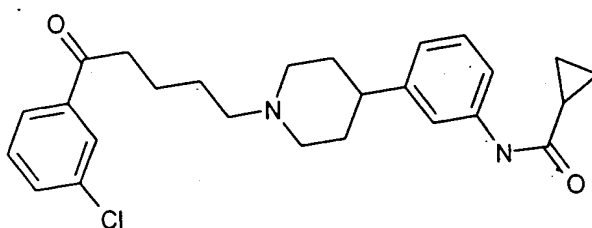
563

50.2



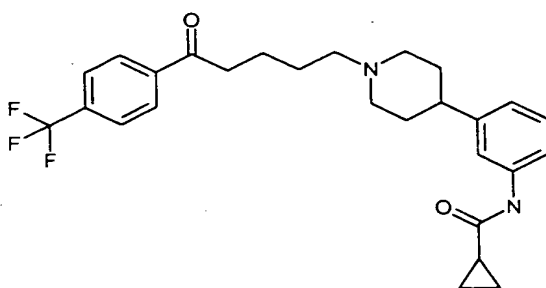
564

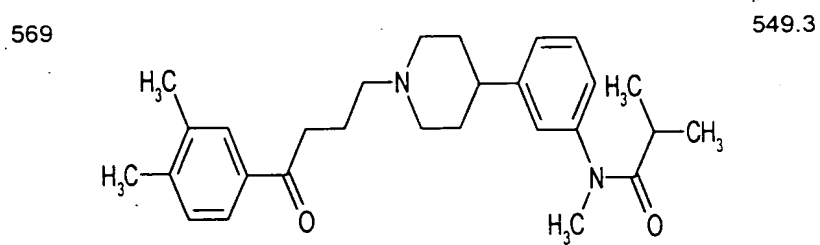
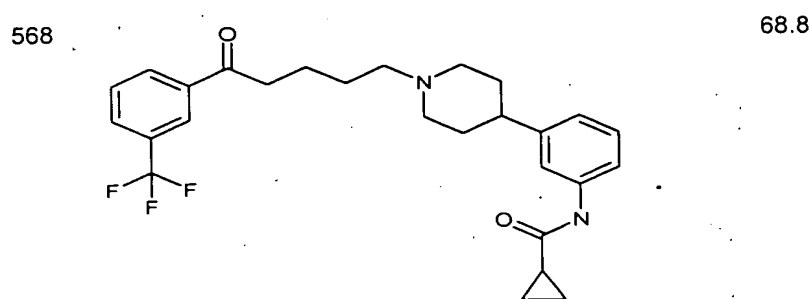
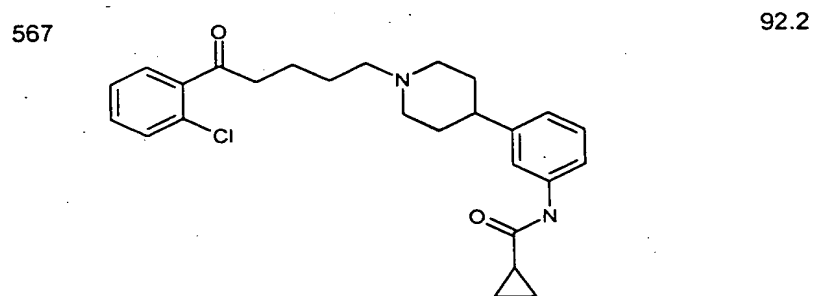
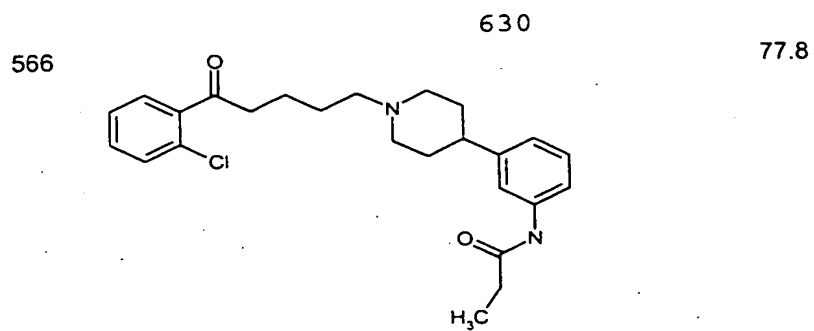
28.9



565

49.2



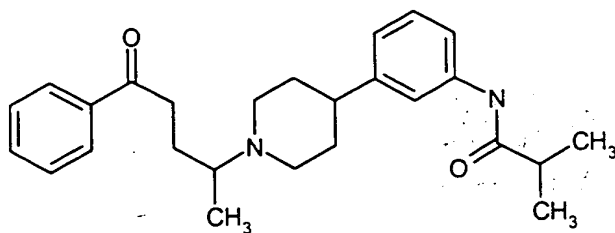




570

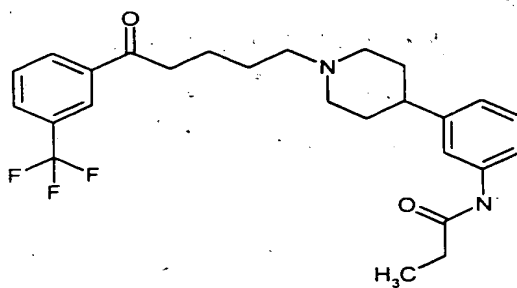
631

136.3



571

88.3



Example

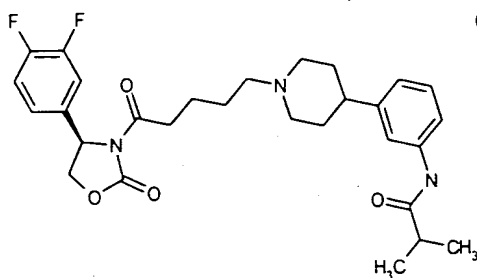
Structure

rMCH1  
Ki (nM)

572

Chiral

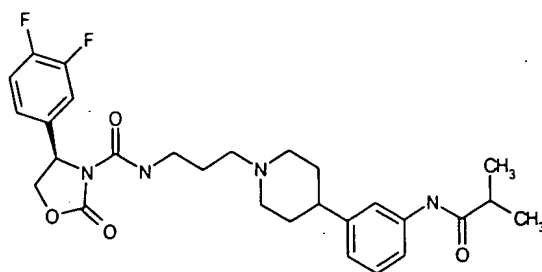
181.5



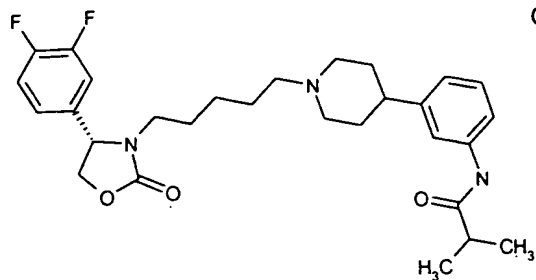
573

Chiral

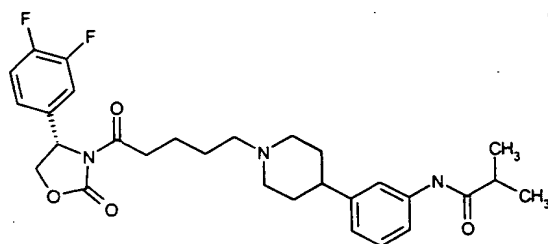
114.3



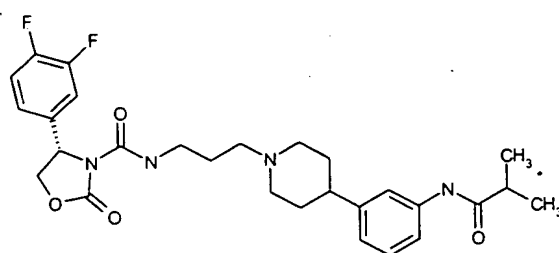
574 632 Chiral 87.1



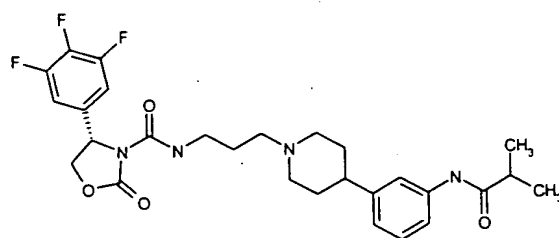
575 Chiral 192.6



576 Chiral 74.3

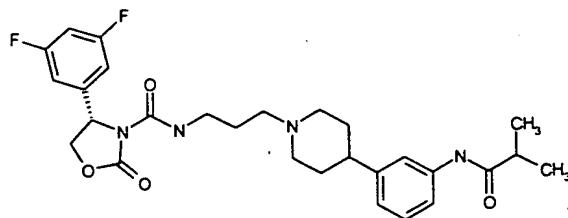


577 Chiral 64.7



633

578



Chiral

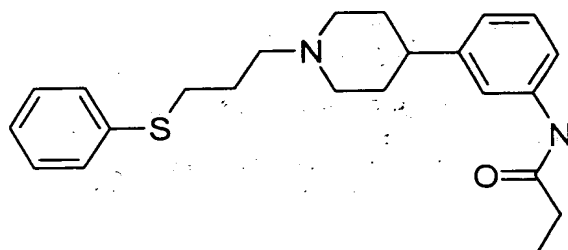
98.8

Example

Structure

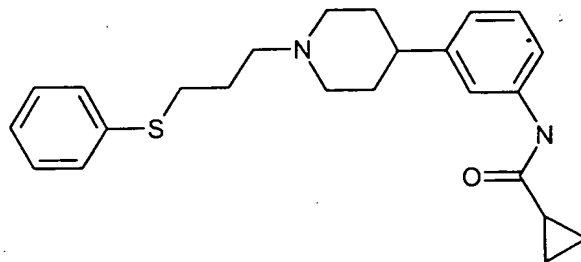
rMCH1  
Ki (nM)

579



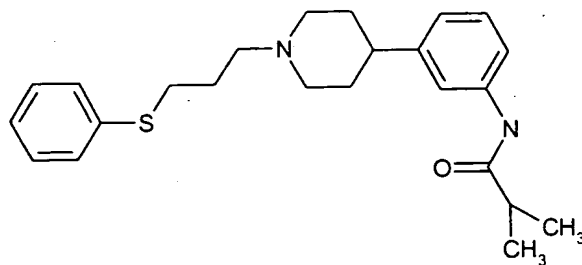
131.1

580



54.0

581

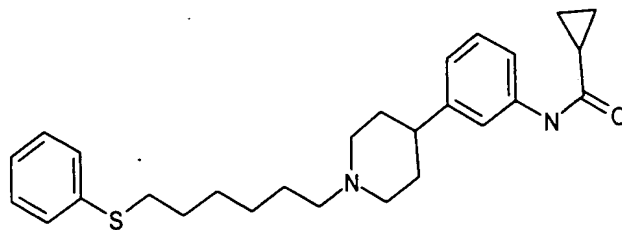


86.4

582

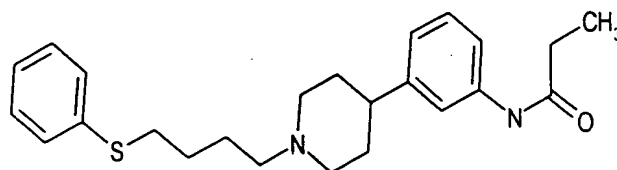
634

58.3



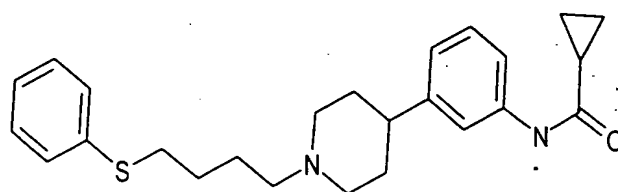
583

55.5



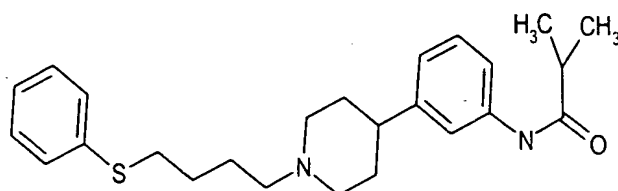
584

51.8

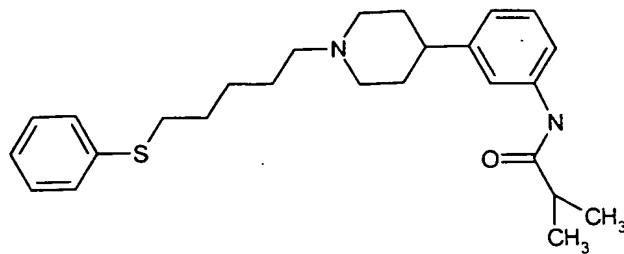


585

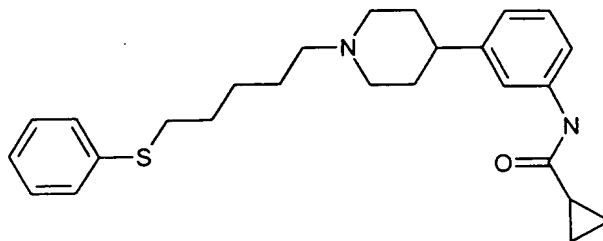
37.2



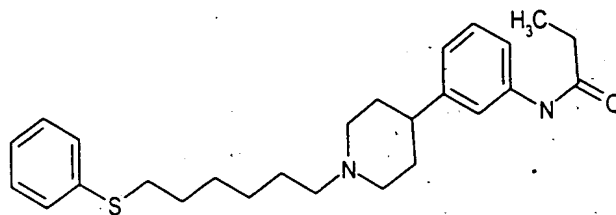
586 635 42.9



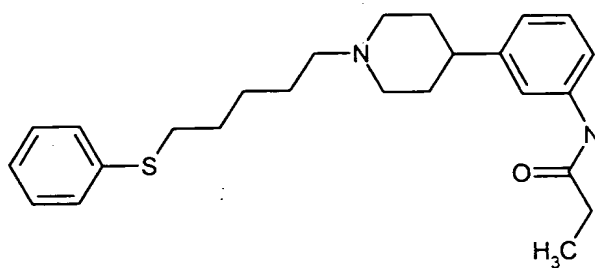
587 46.9

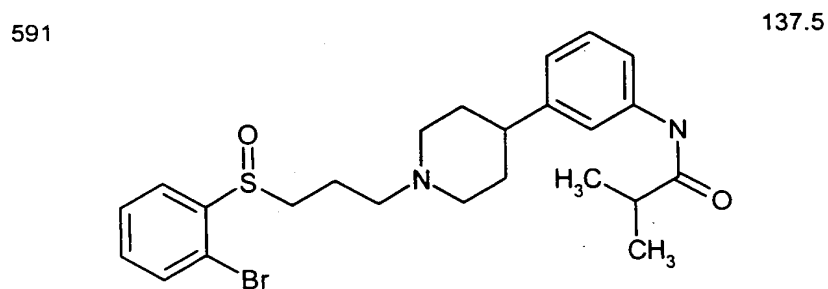
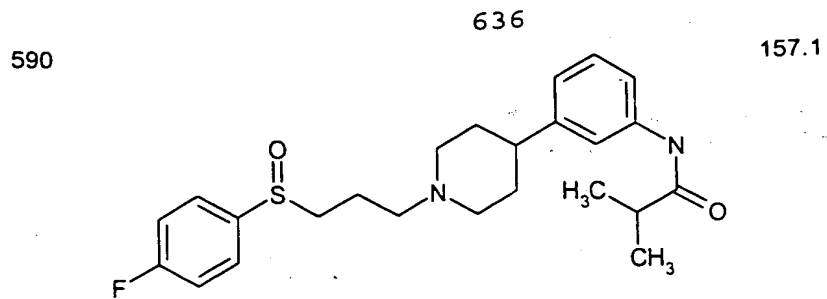


588 283.9



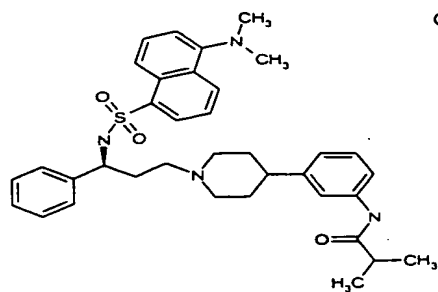
589 66.6



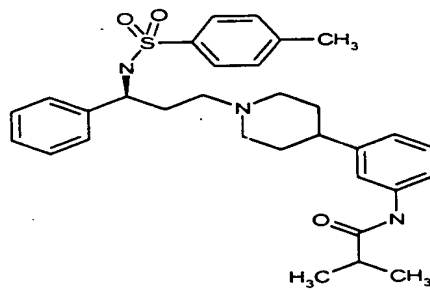


Example	Structure		rMCH1 Ki (nM)
592		Chiral	185.6
593		Chiral	7.6

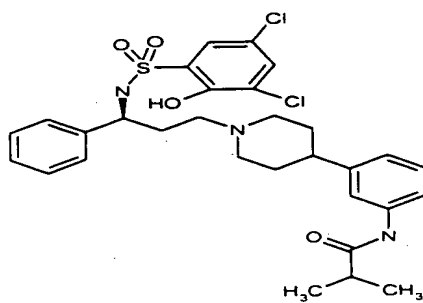
594 637 Chiral 67.0



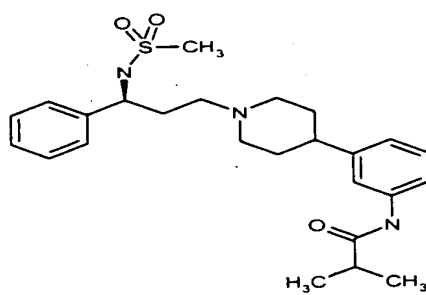
595 Chiral 36.3



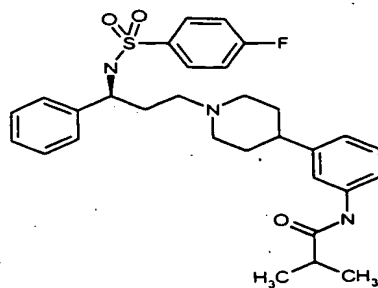
596 Chiral 596.7



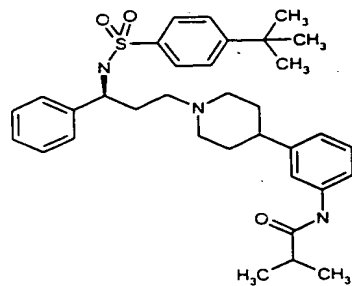
597 Chiral 222.7



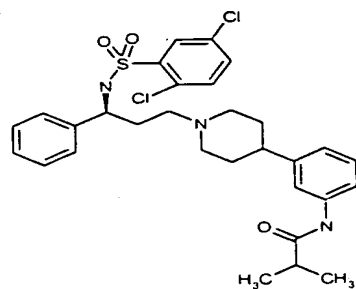
598 638 Chiral 25.3



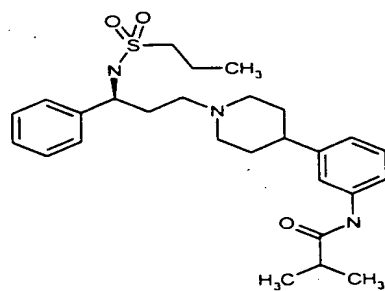
599 Chiral 50.0



600 Chiral 41.3



601 Chiral 144.2



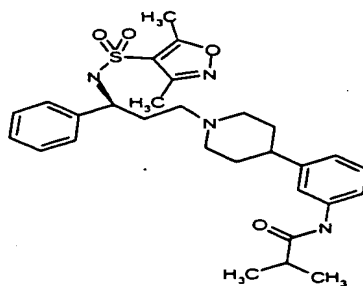


602

639

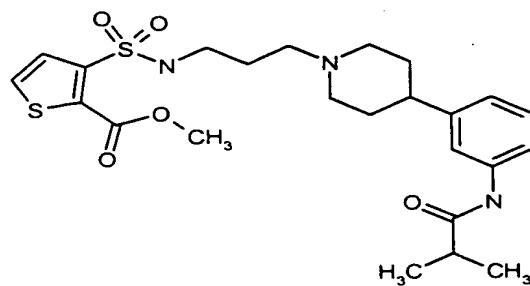
Chiral

44.6



603

286.8



### Example

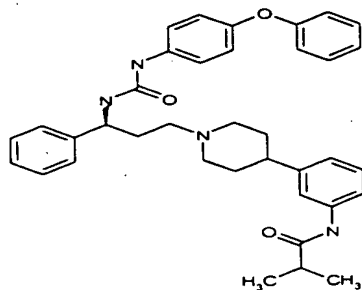
MOLSTRUCTURE

rMCH1	Ki (nM)
1	100
2	100
3	100
4	100
5	100
6	100
7	100
8	100
9	100
10	100
11	100
12	100
13	100
14	100
15	100
16	100
17	100
18	100
19	100
20	100
21	100
22	100
23	100
24	100
25	100
26	100
27	100
28	100
29	100
30	100
31	100
32	100
33	100
34	100
35	100
36	100
37	100
38	100
39	100
40	100
41	100
42	100
43	100
44	100
45	100
46	100
47	100
48	100
49	100
50	100
51	100
52	100
53	100
54	100
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56	100
57	100
58	100
59	100
60	100
61	100
62	100
63	100
64	100
65	100
66	100
67	100
68	100
69	100
70	100
71	100
72	100
73	100
74	100
75	100
76	100
77	100
78	100
79	100
80	100
81	100
82	100
83	100
84	100
85	100
86	100
87	100
88	100
89	100
90	100
91	100
92	100
93	100
94	100
95	100
96	100
97	100
98	100
99	100
100	100

604

**Chiral**

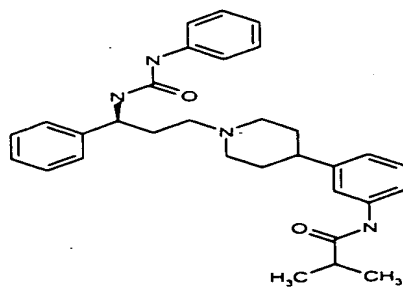
36.8\_

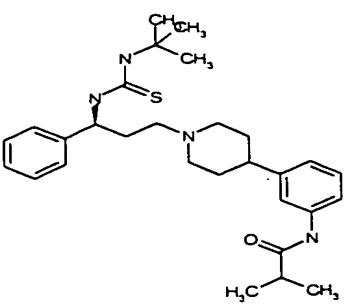
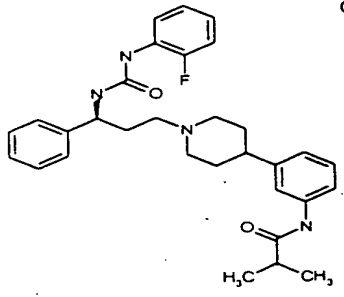
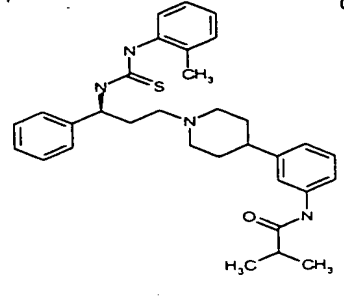
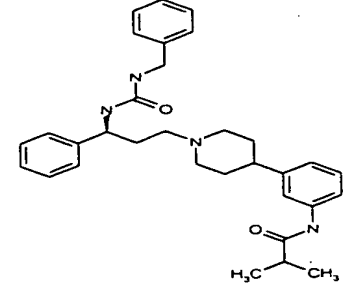


605

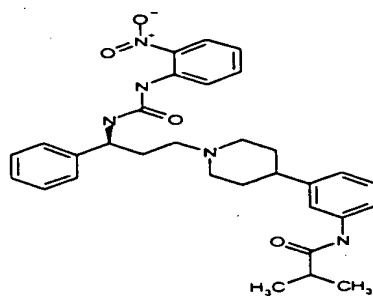
Chiral

94.5

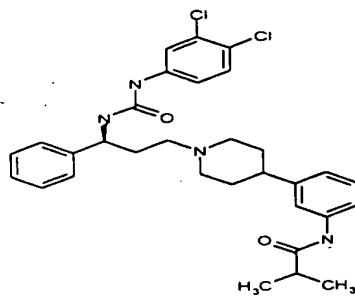


606		640 Chiral	40.4
607		Chiral	142.1
608		Chiral	34.9
609		Chiral	35.4

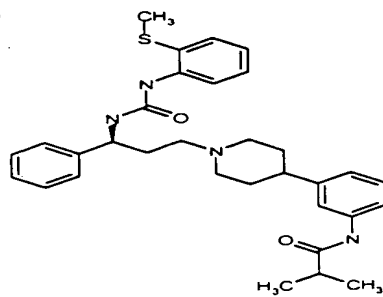
610 641 529.8  
Chiral



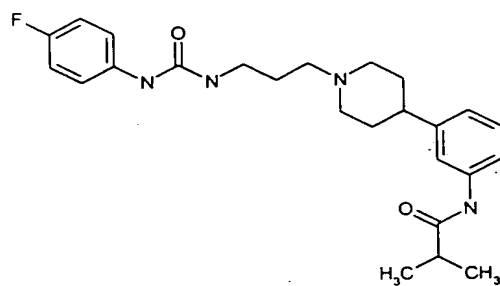
611 65.1  
Chiral



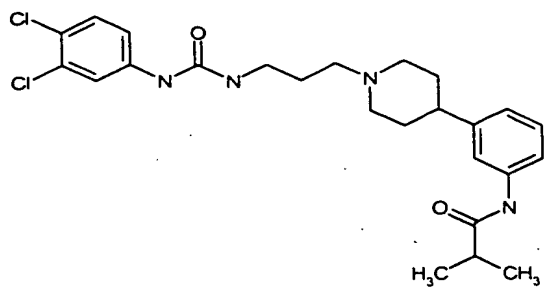
612 121.0  
Chiral



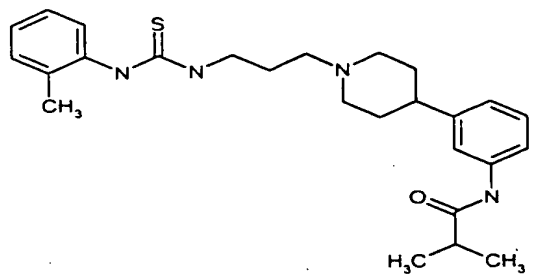
613 34.9



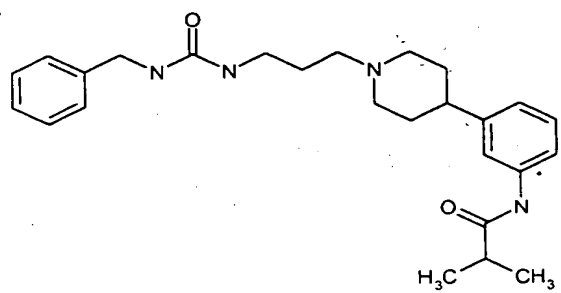
614 642 84.8



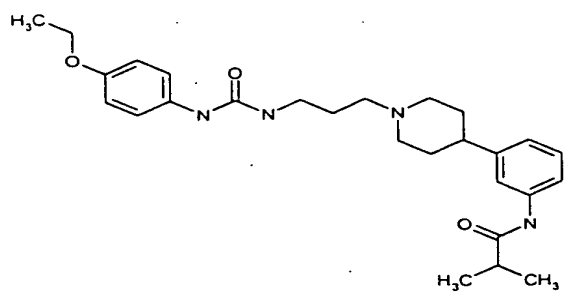
615 210.5

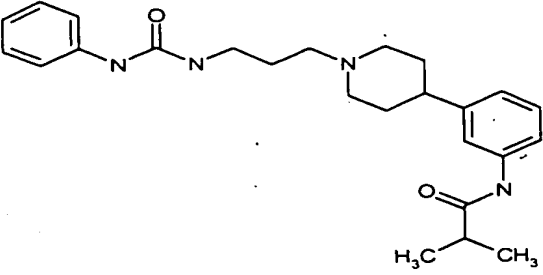
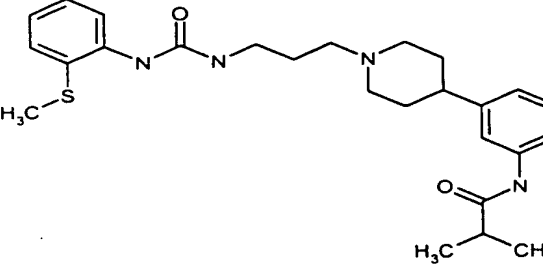
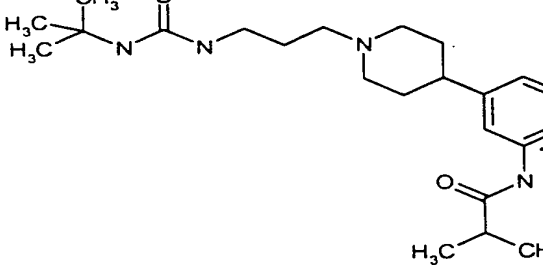
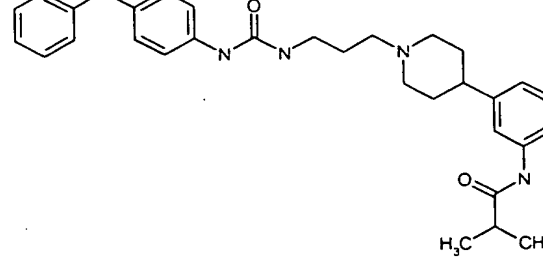


616 405.6



617 608.9



618		643	399.5
619			177.5
620			223.3
621			204.6

Example

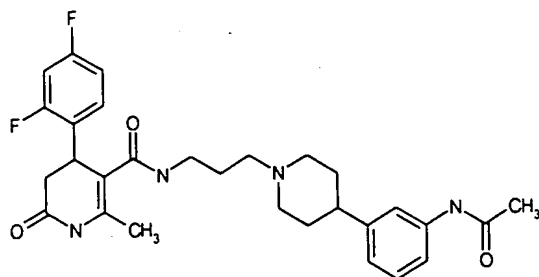
Structure

rMCH1  
Ki (nM)

644

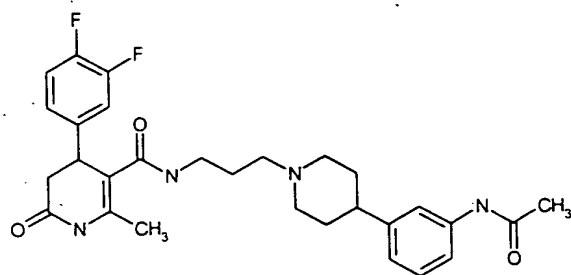
622

162.4



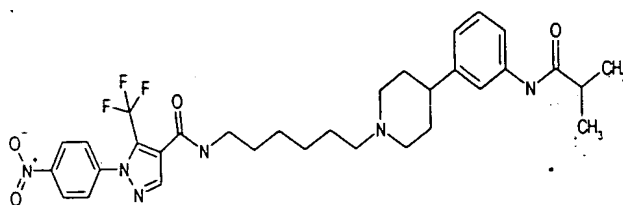
623

23.1



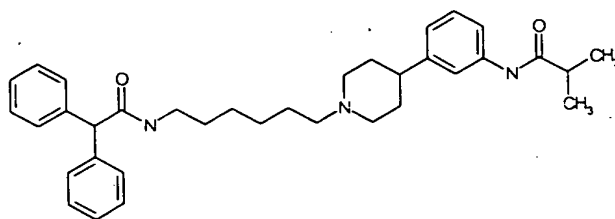
624

47.8



625

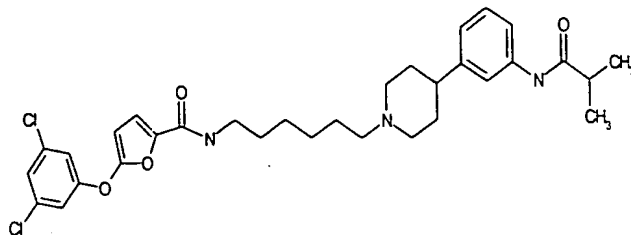
29.5



626

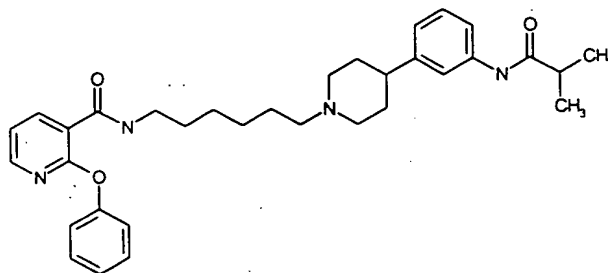
645

20.9



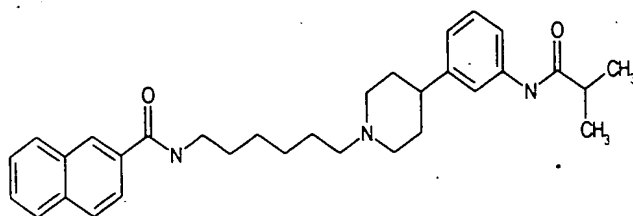
627

109.1



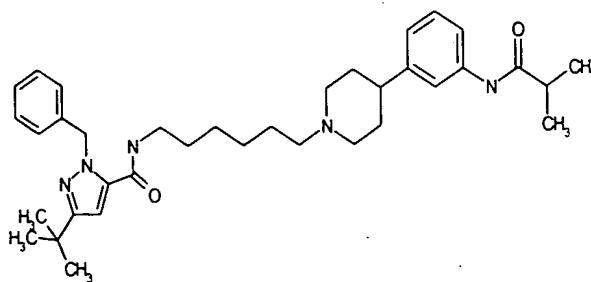
628

160.6



629

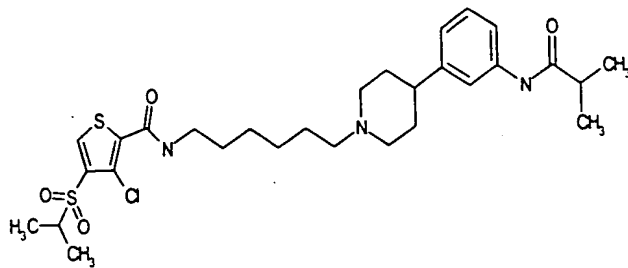
42.9



630

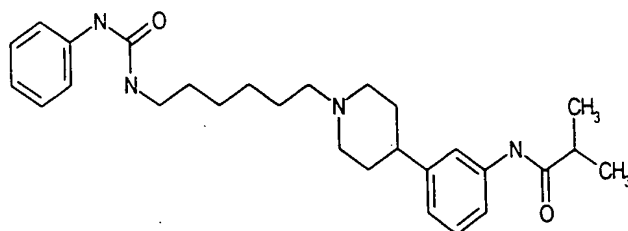
646

201.8



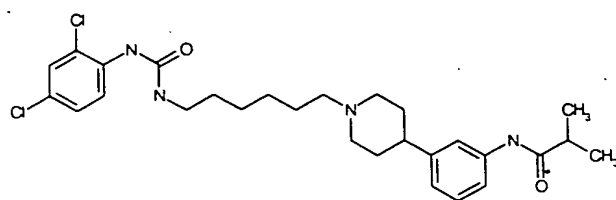
631

258.8



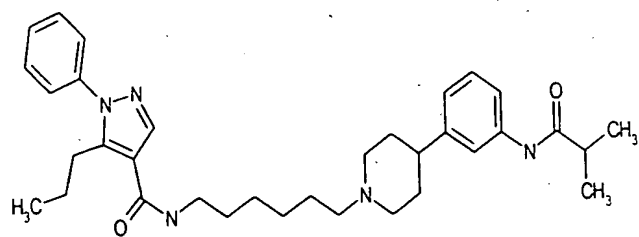
632

76.6



633

107.9

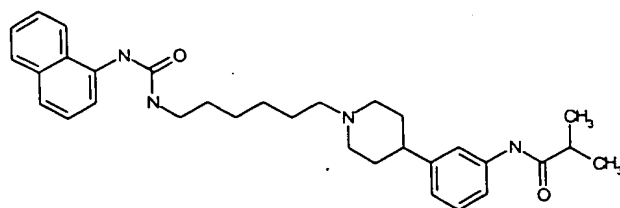




647

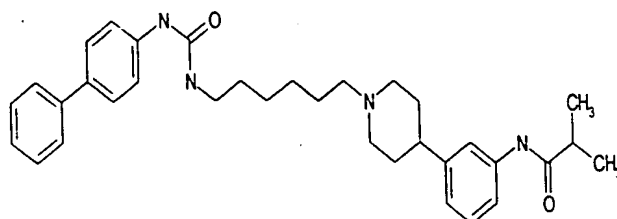
116.1

634



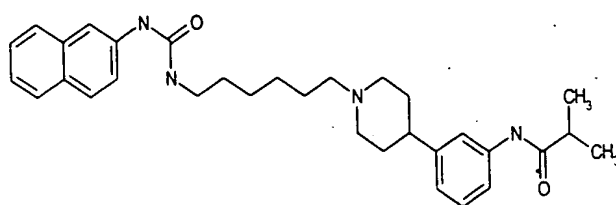
73.6

635



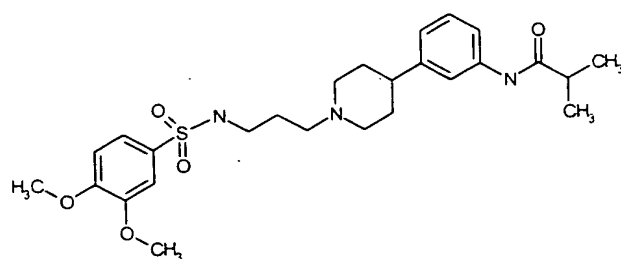
40.8

636



105.6

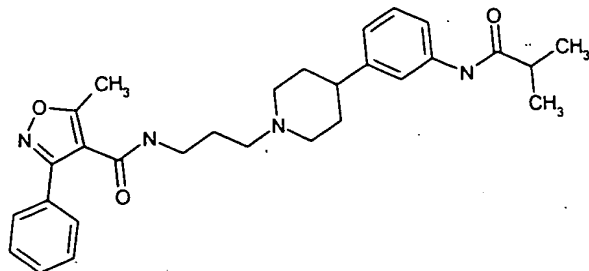
637



638

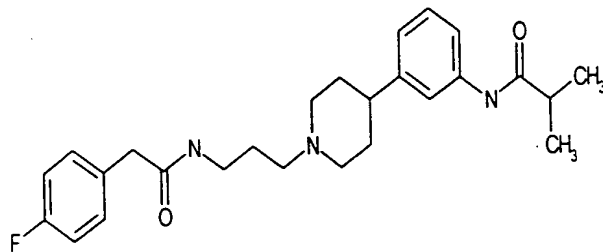
648

29.8



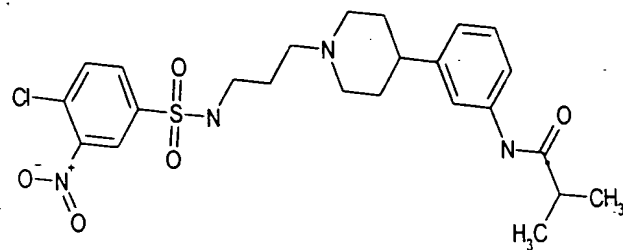
639

36.3



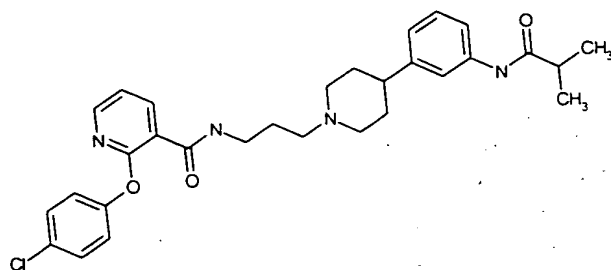
640

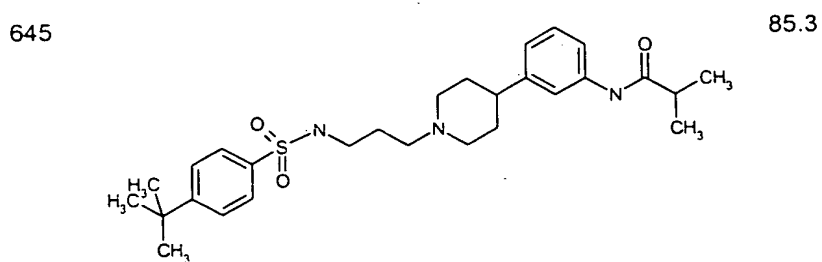
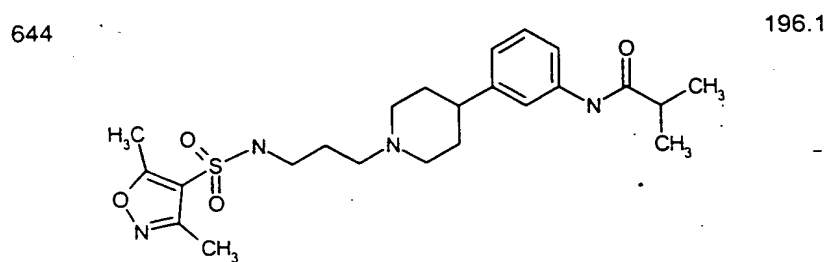
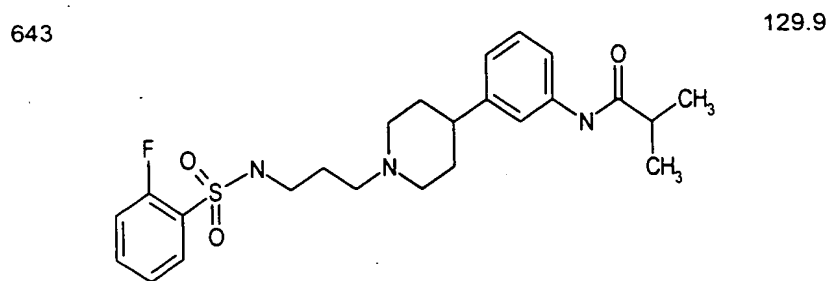
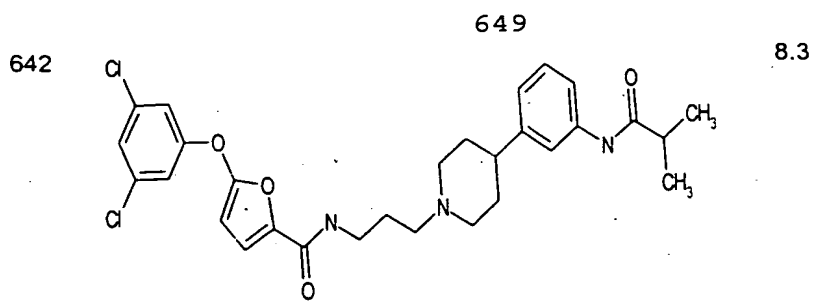
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641

14.2

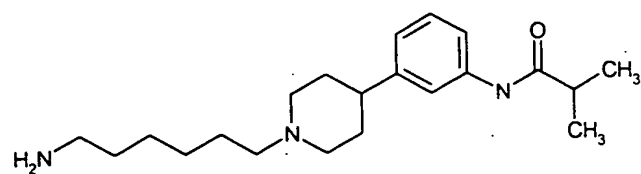




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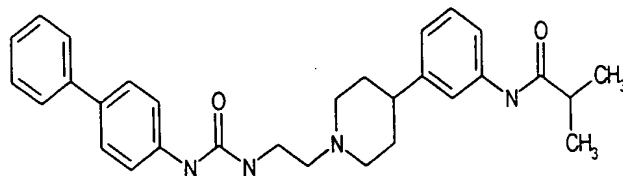
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235.7



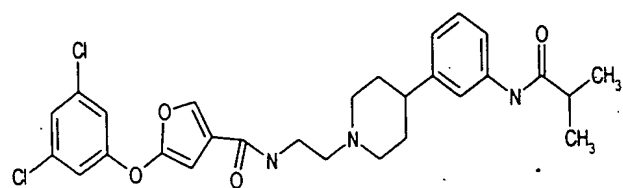
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81.6



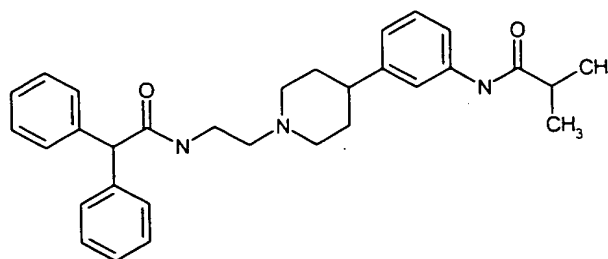
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13.4



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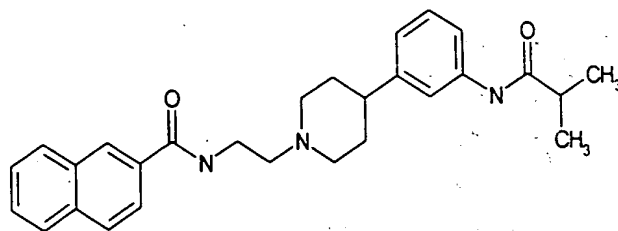
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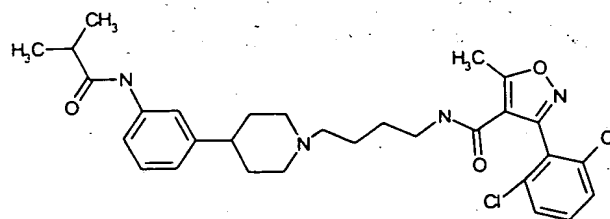
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21.1



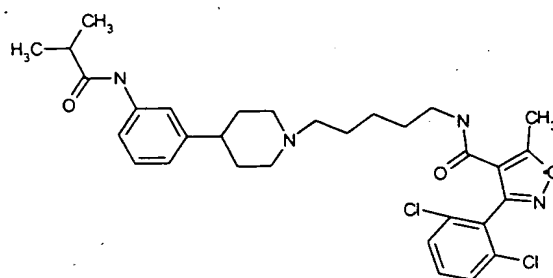
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16.7



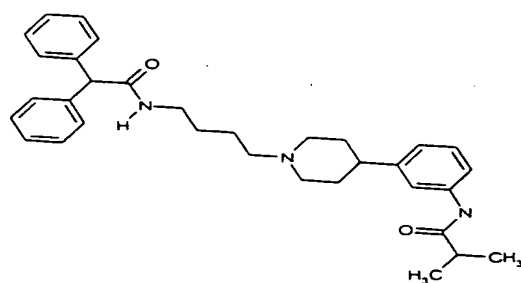
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7.1

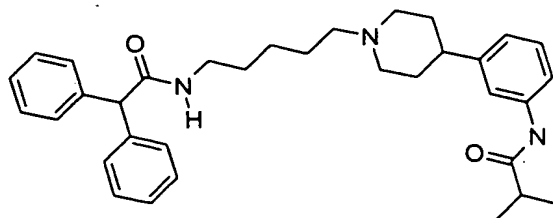


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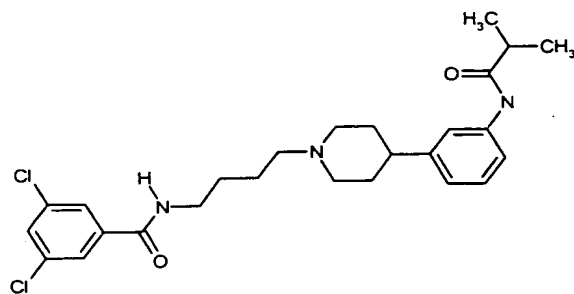
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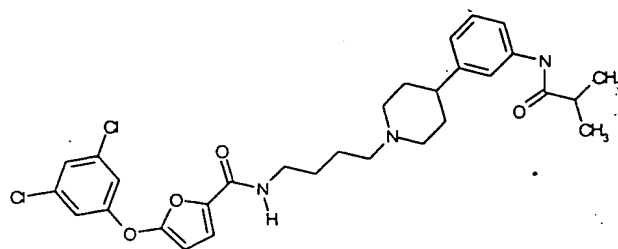
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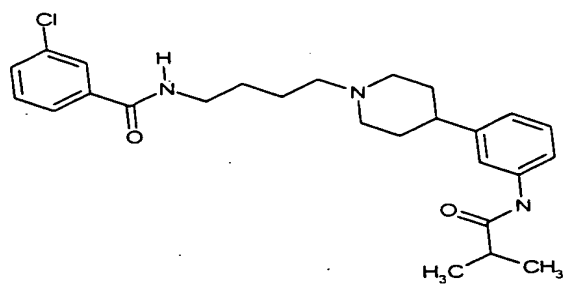
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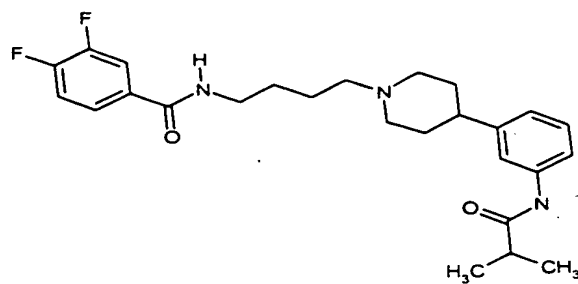
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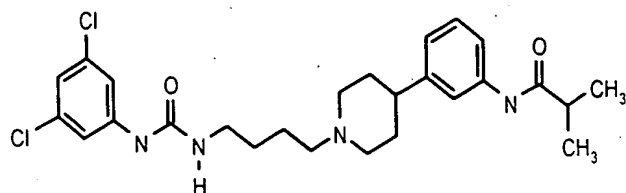
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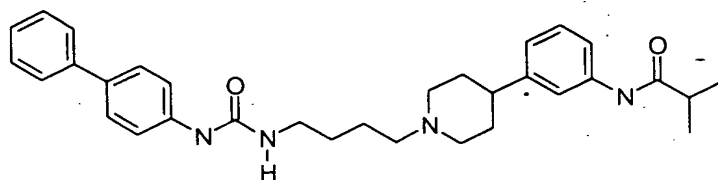
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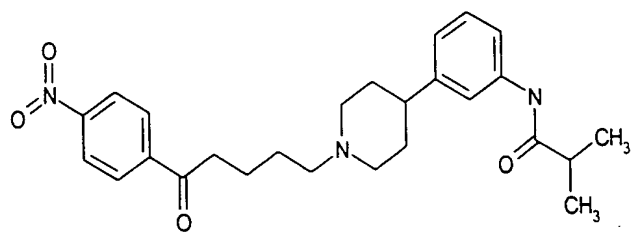
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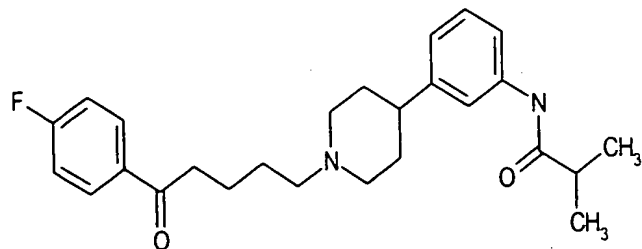
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661 33.3

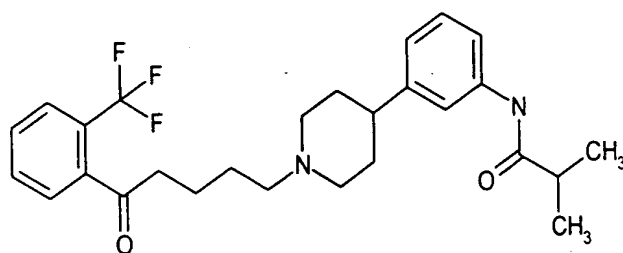


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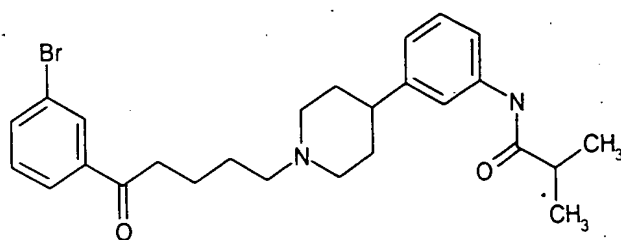
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73.4



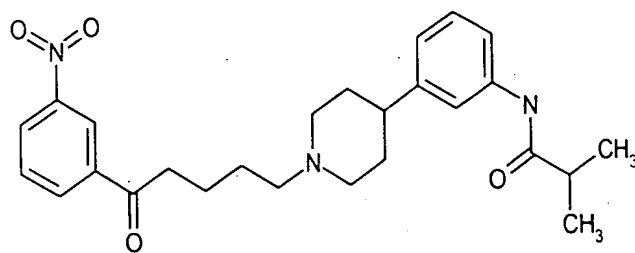
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21.9



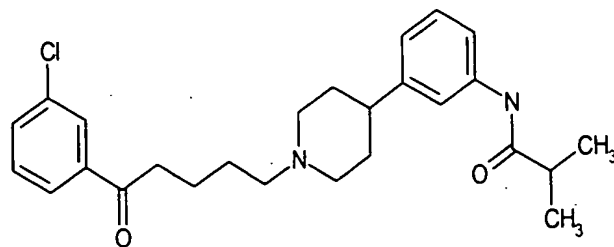
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38.4

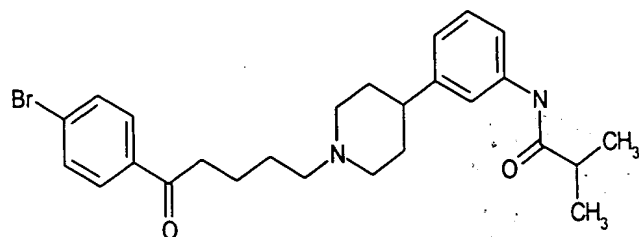




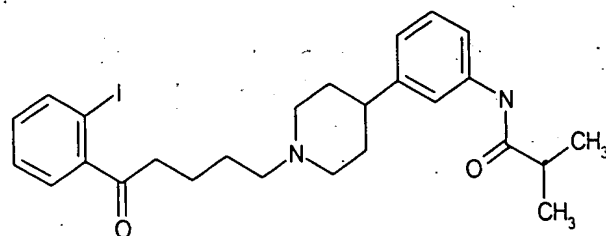
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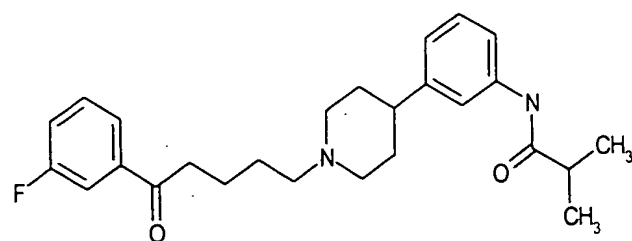
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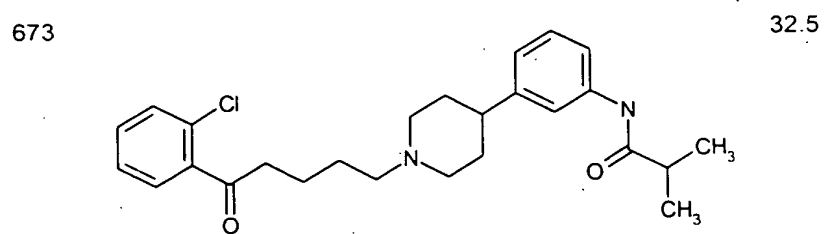
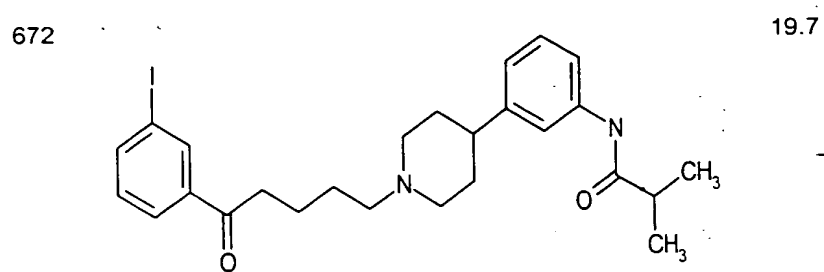
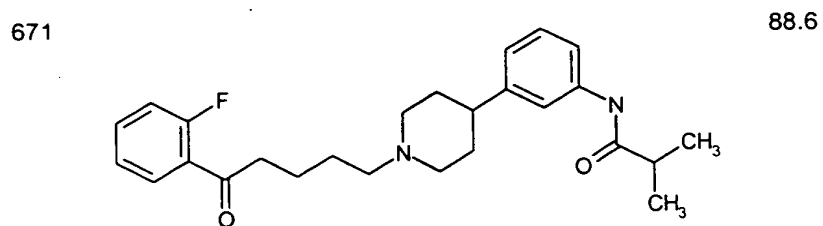
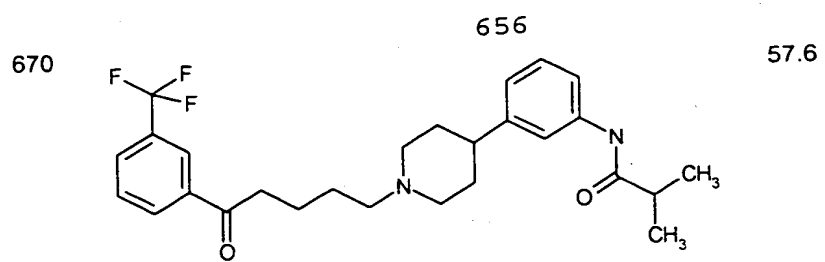


668 25.8



669 42.2

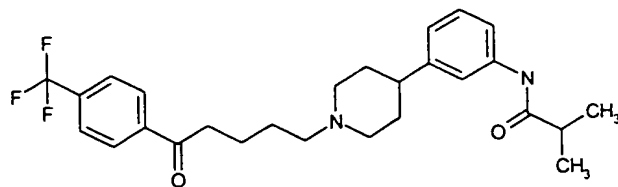




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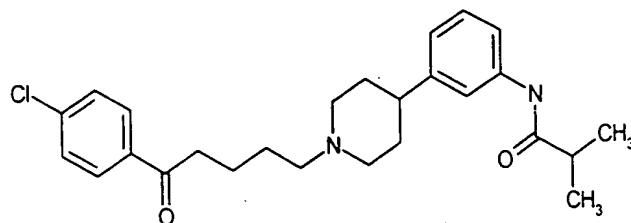
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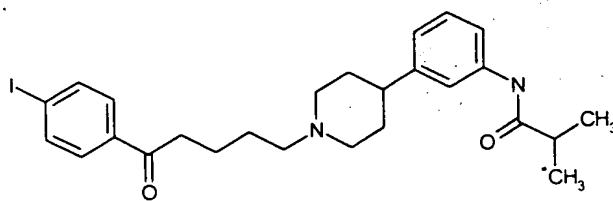
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32.6



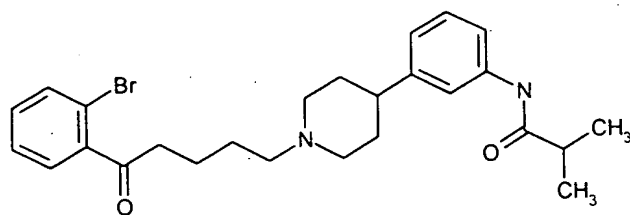
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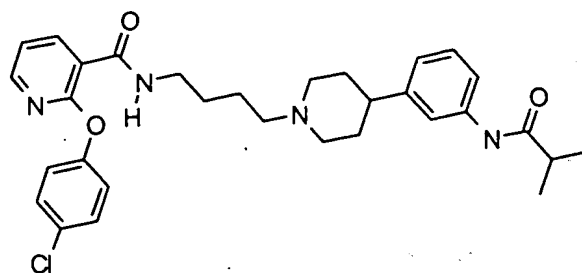


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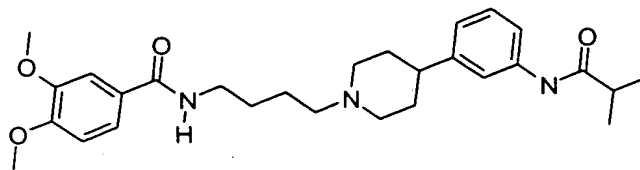
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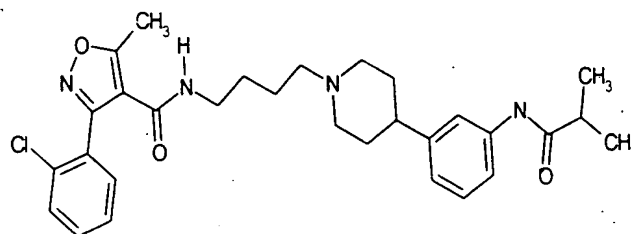
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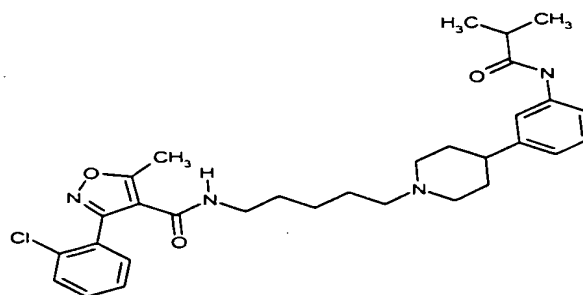
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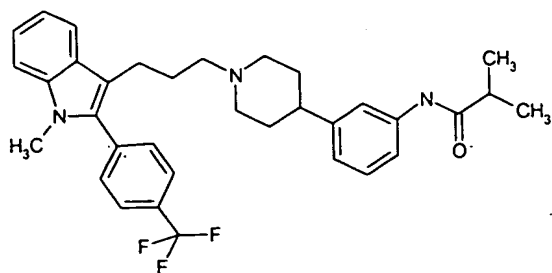
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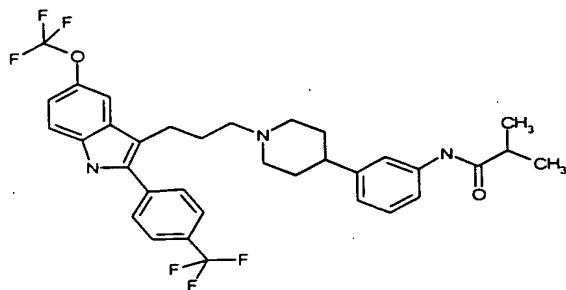
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## 7.1



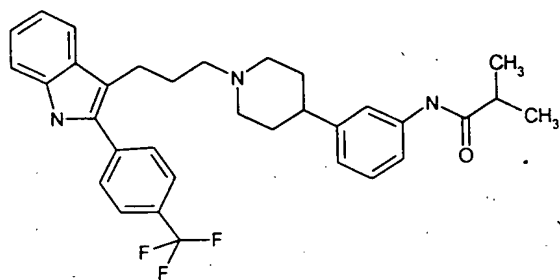
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54.2



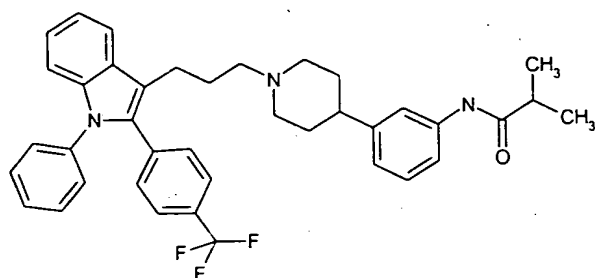
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## 5.4

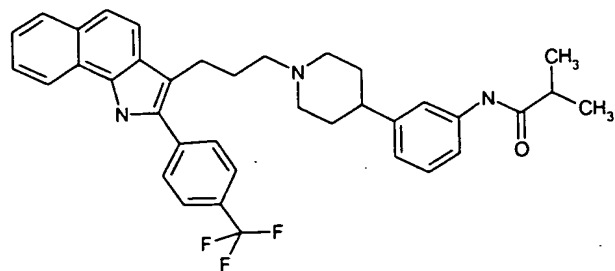


685

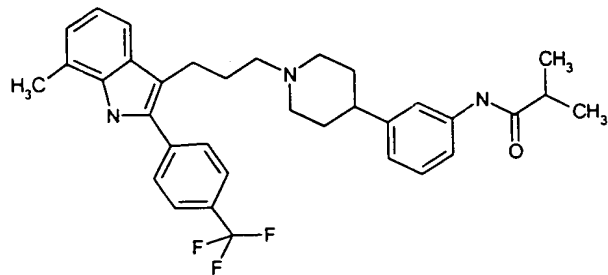
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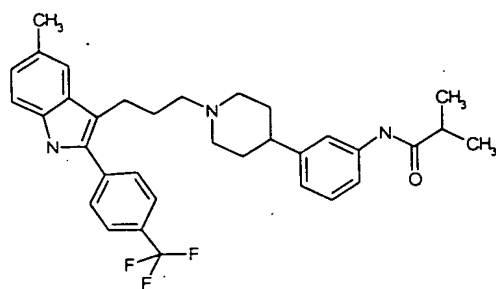
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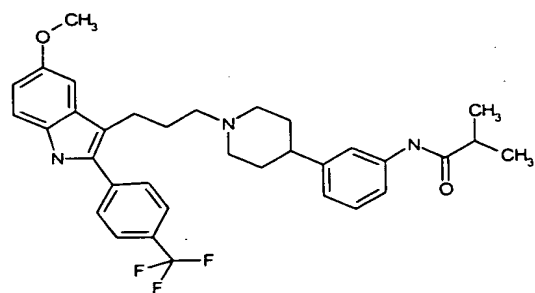
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688 41.0



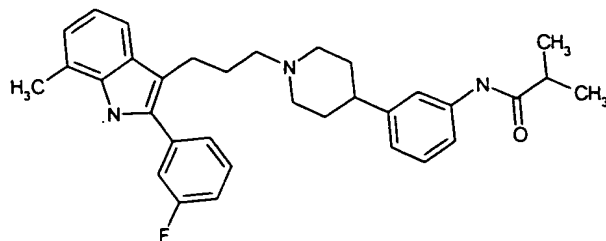
689 11.3



690

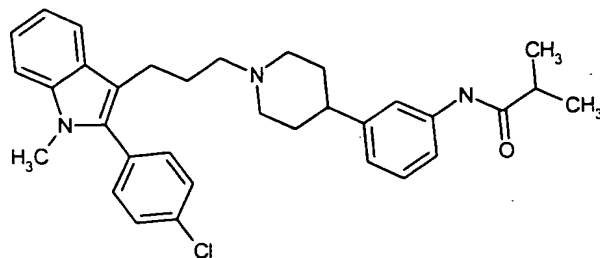
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5.2



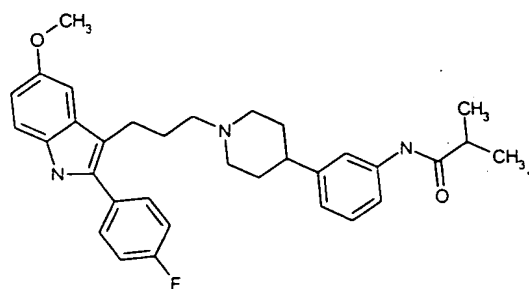
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16.3



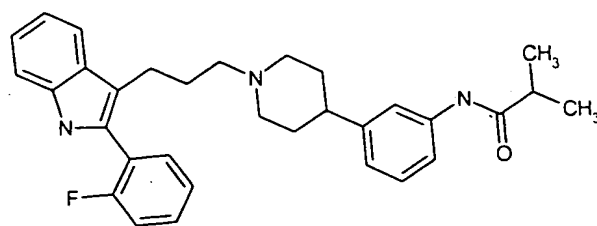
692

2.0



693

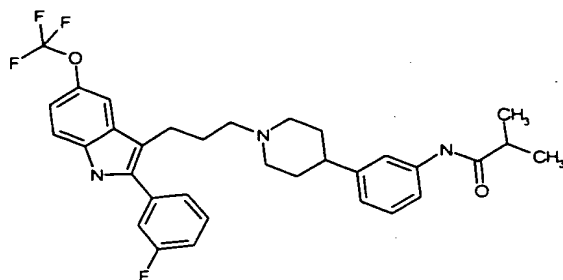
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662

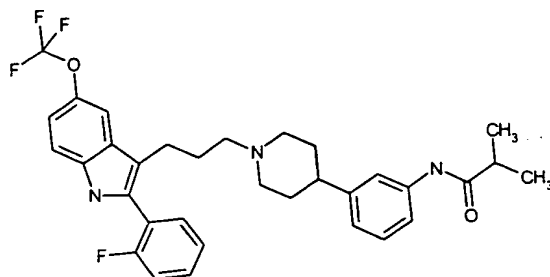
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694



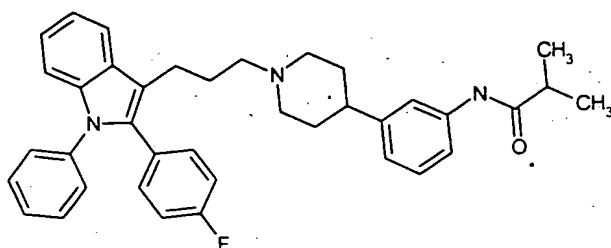
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2.1



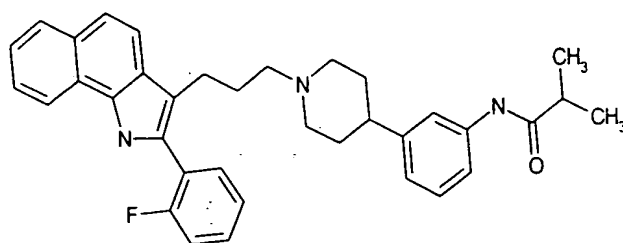
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48.3



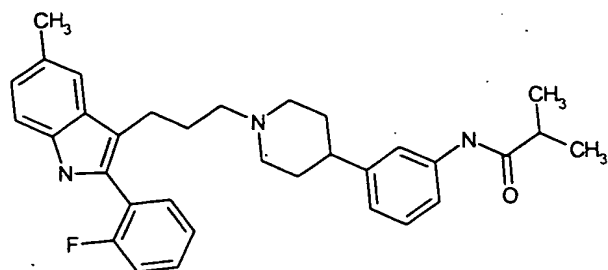
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3.0

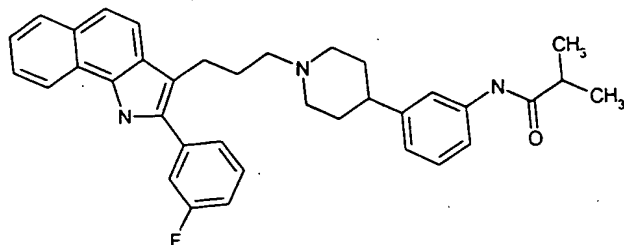




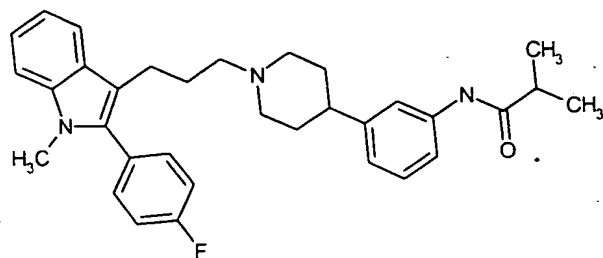
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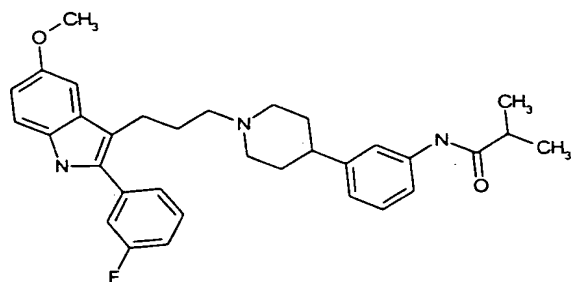
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700 2.0



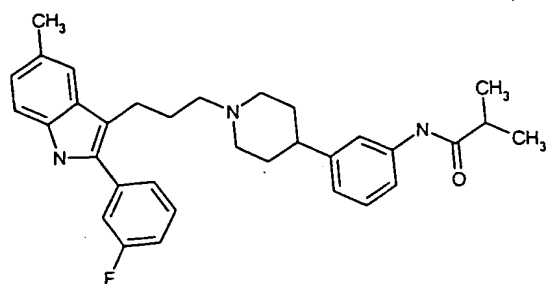
701 2.5





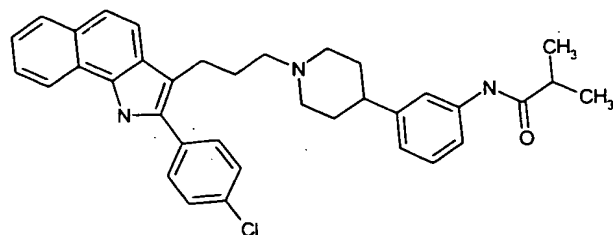
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4.2



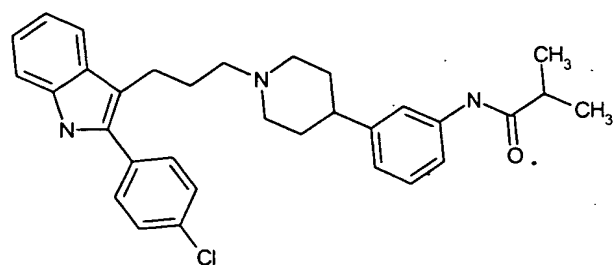
707

19.6



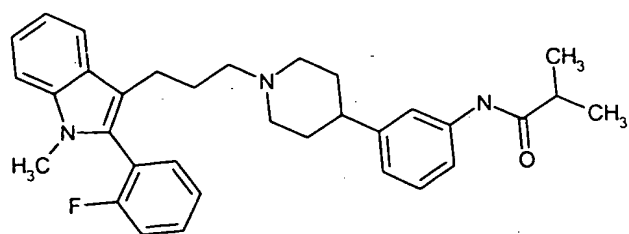
708

3.8

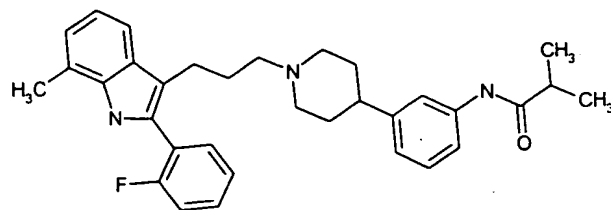


709

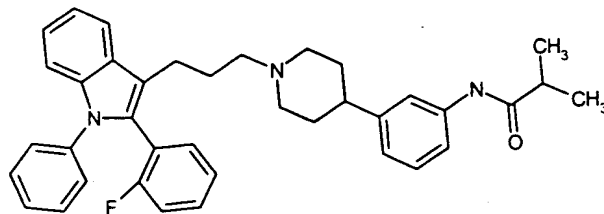
1.3



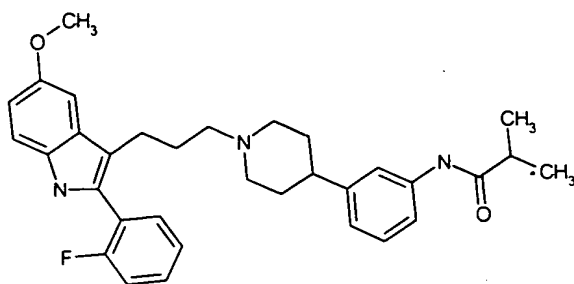
710 666 6.9



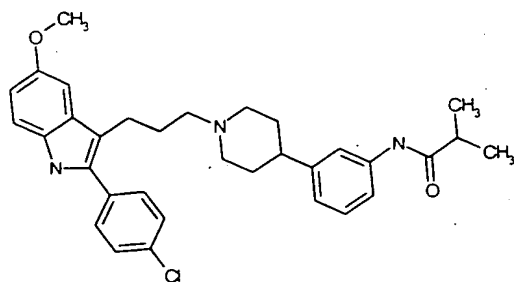
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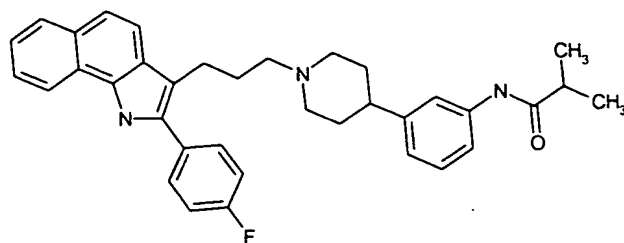
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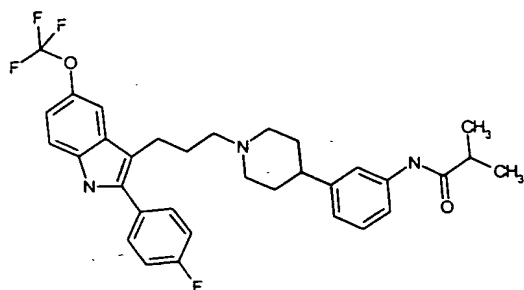
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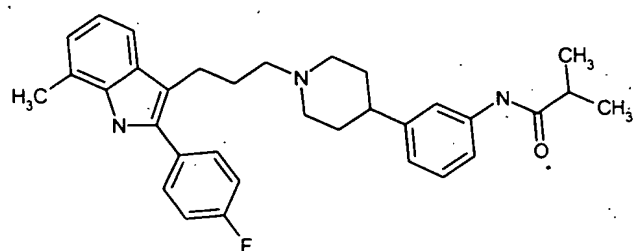
714 667 4.7



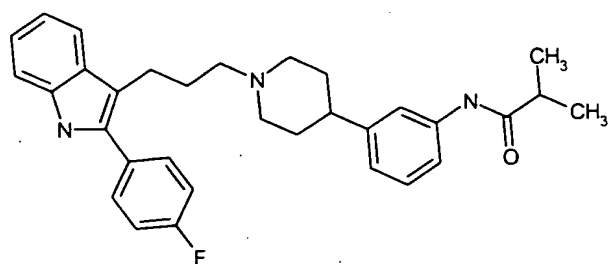
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716 4.5



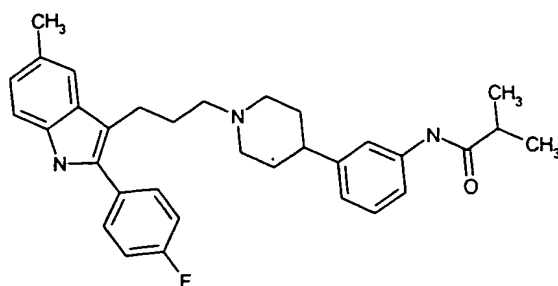
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668

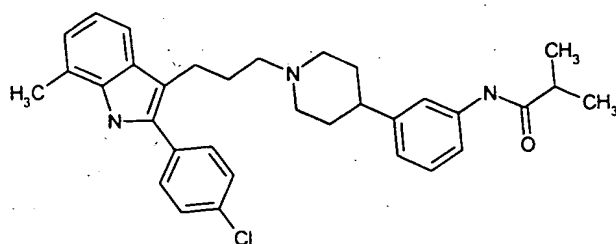
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3.4



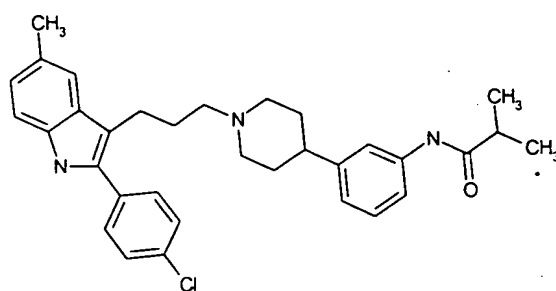
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14.9



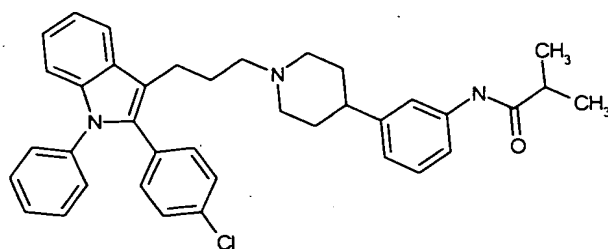
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12.5



721

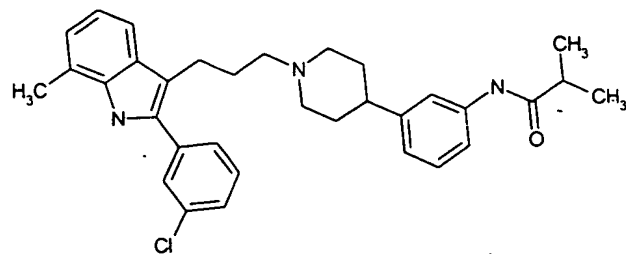
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669

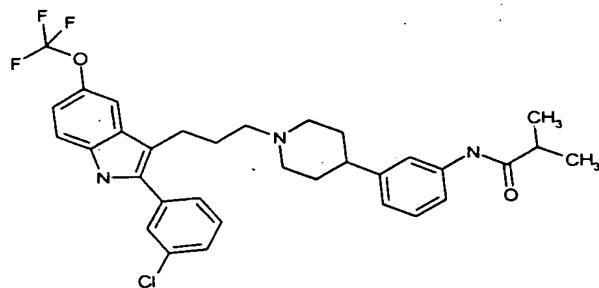
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6.4



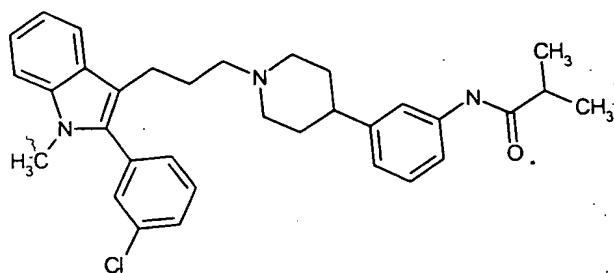
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9.2



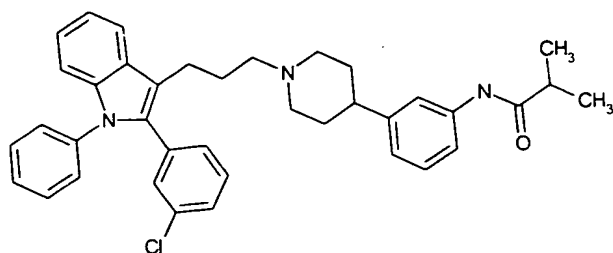
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5.0



725

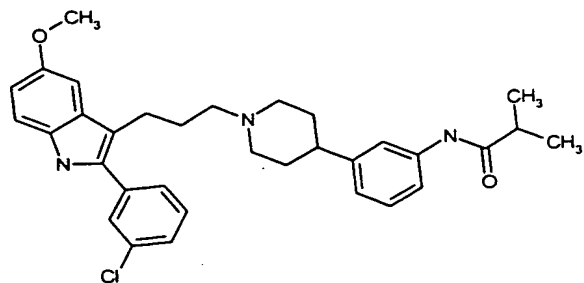
151.6



670

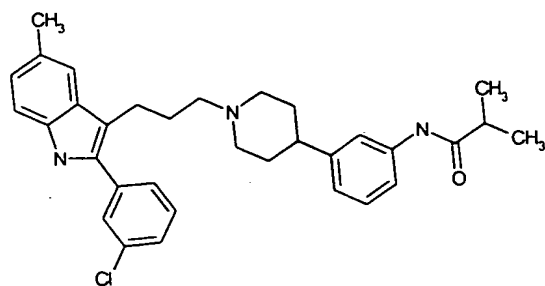
726

5.0



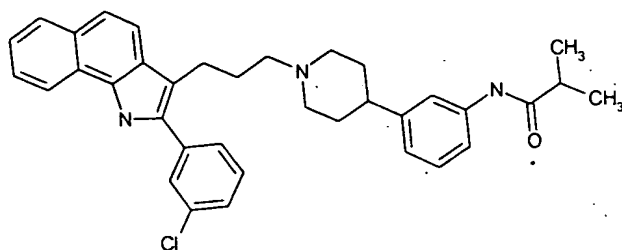
727

3.4



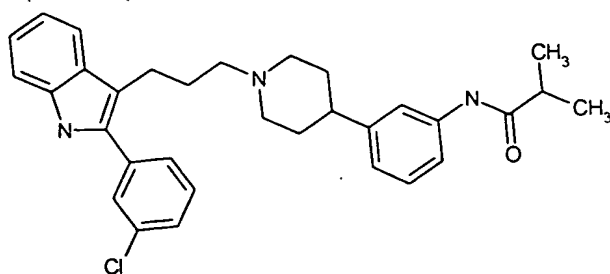
728

16.3



729

1.7

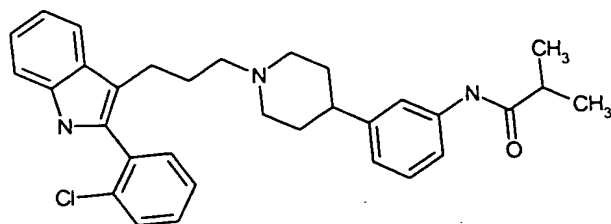




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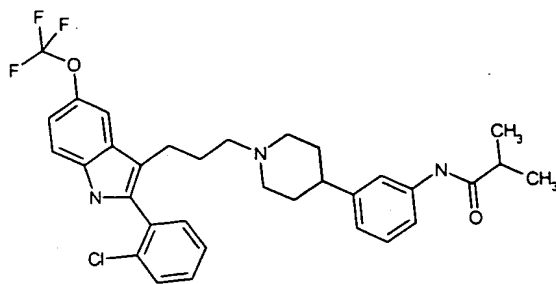
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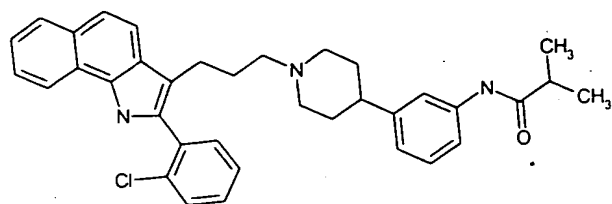
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9.9



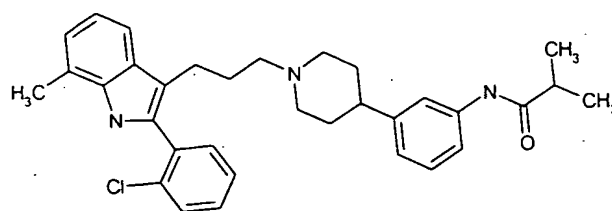
732

5.8



733

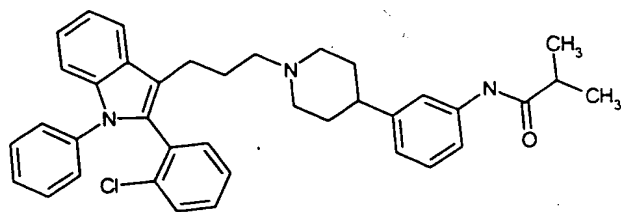
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734

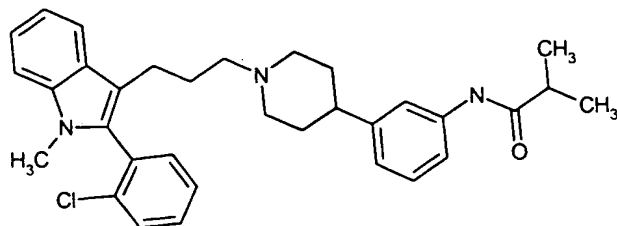
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28.6



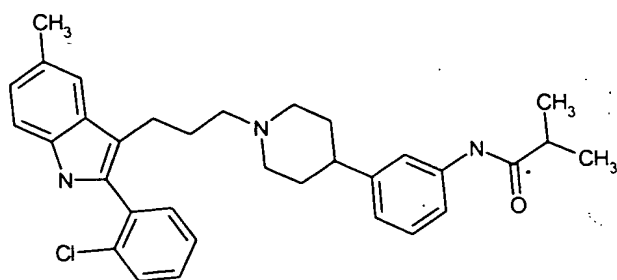
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1.1



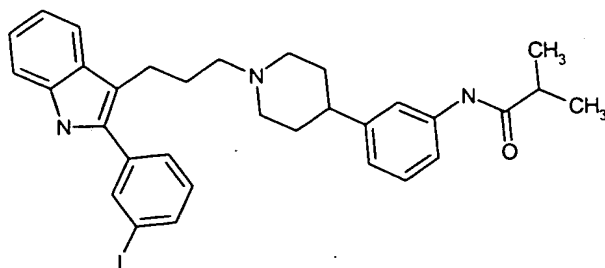
736

5.7

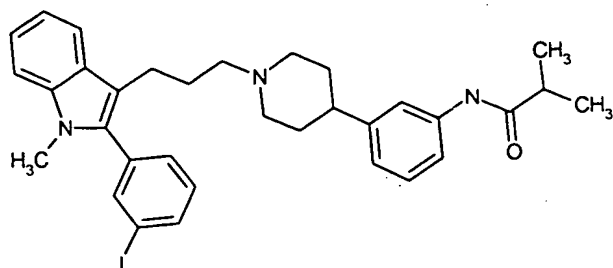


737

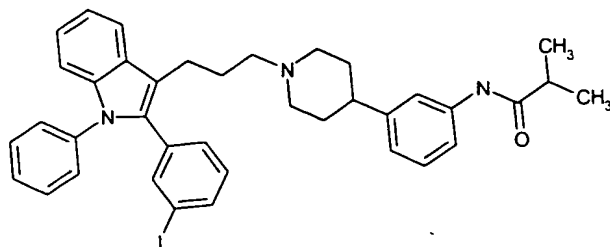
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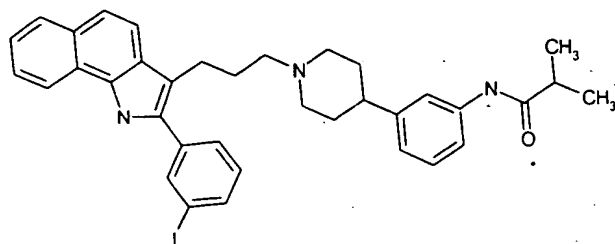
738 673 10.2



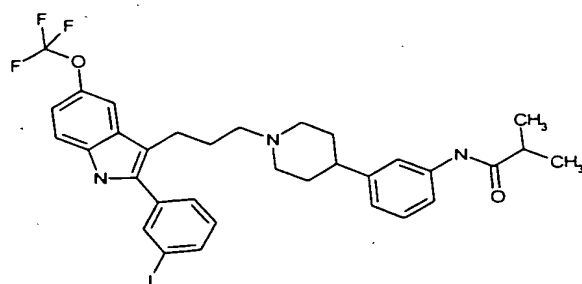
739 213.6



740 12.2



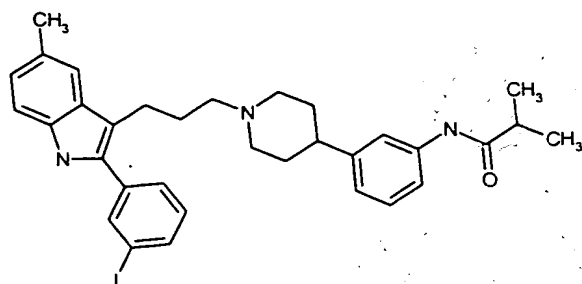
741 2.8



674

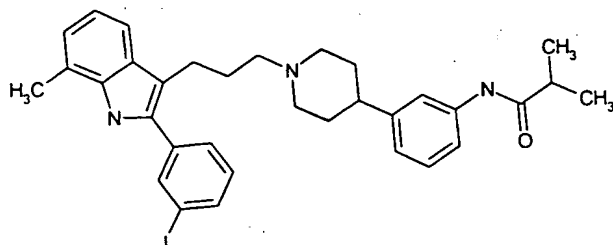
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1.4



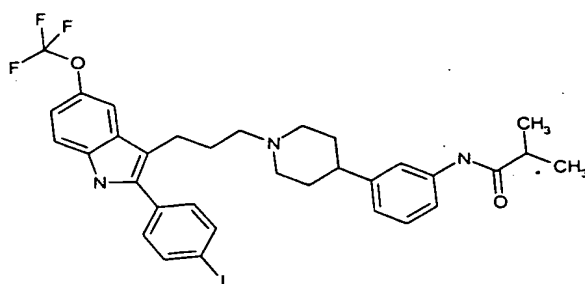
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4.1



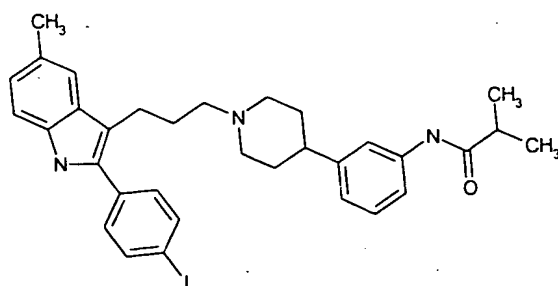
744

47.1



745

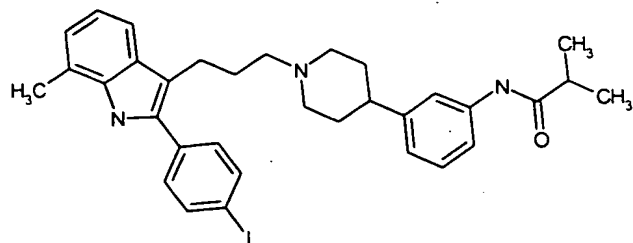
15.8



746

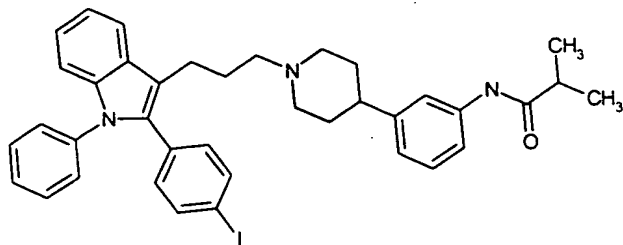
675

8.0



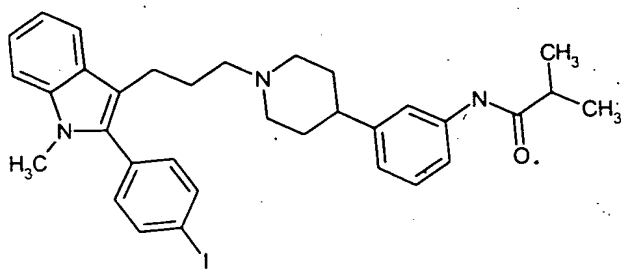
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160.6



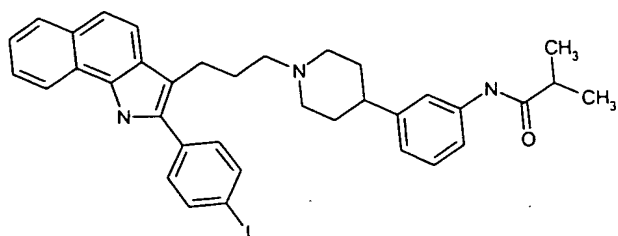
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3.1



749

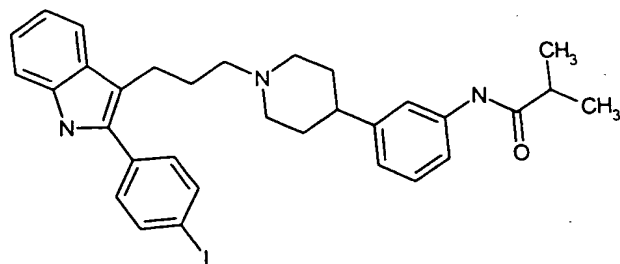
23.2



676

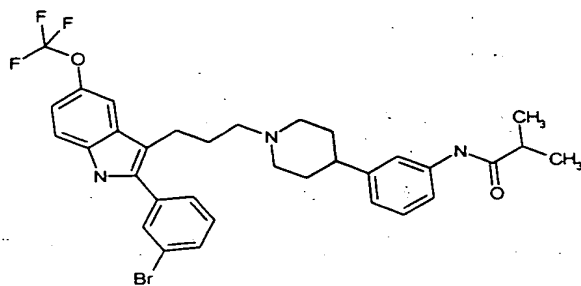
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2.6



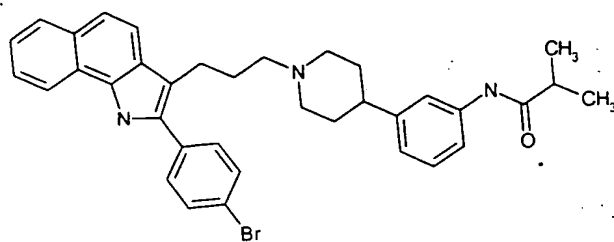
751

12.4



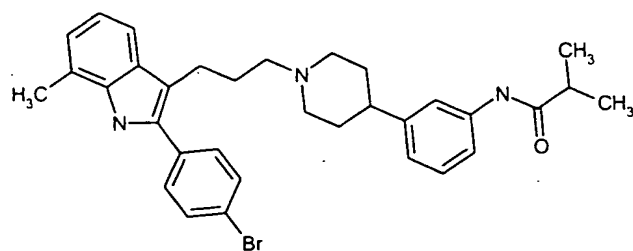
752

21.7



753

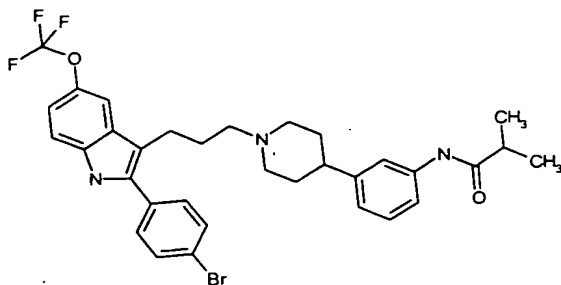
16.6



677

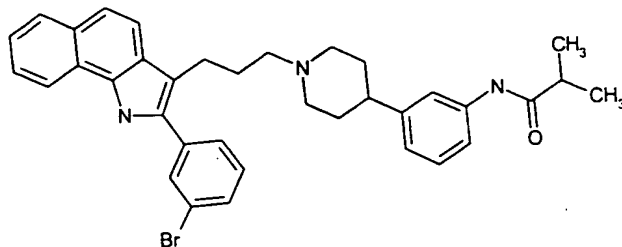
49.2

754



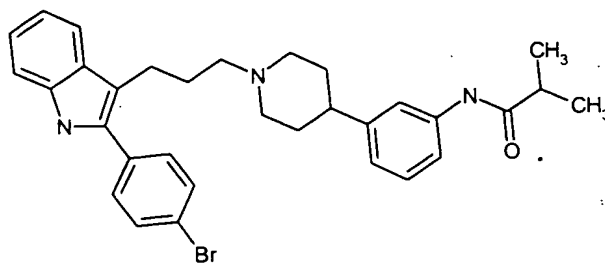
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755



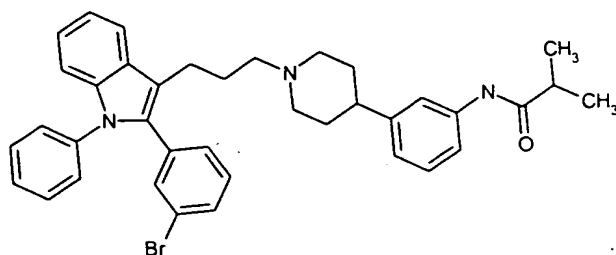
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756



6.9

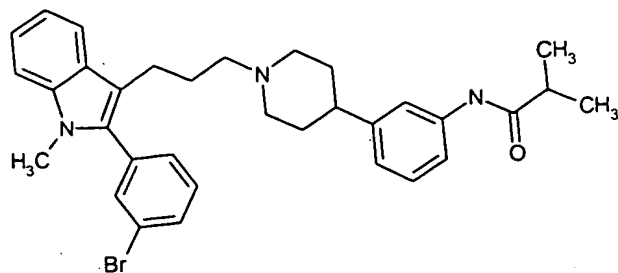
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758

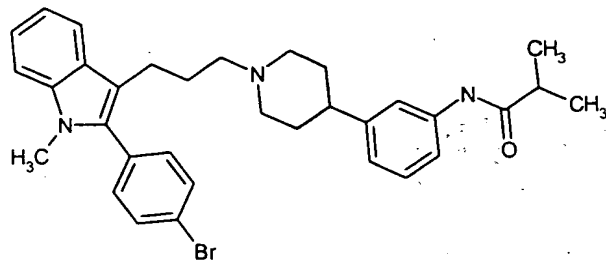
678

110.0



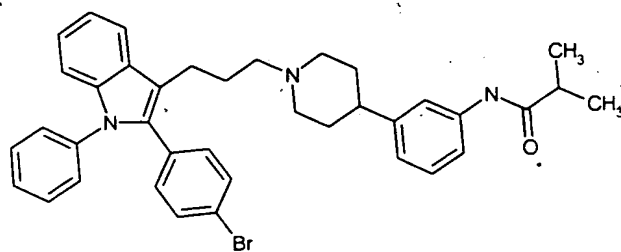
759

9.3



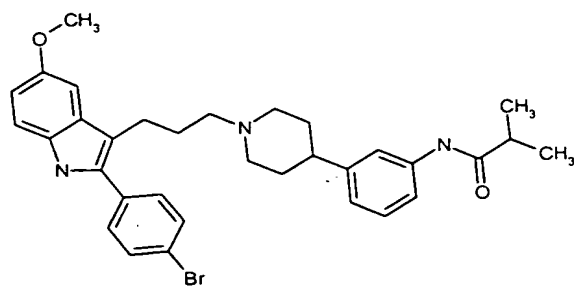
760

92.3



761

15.9

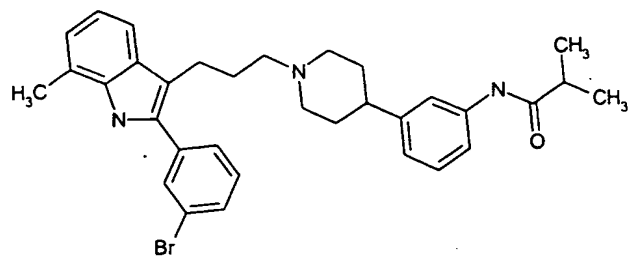




679

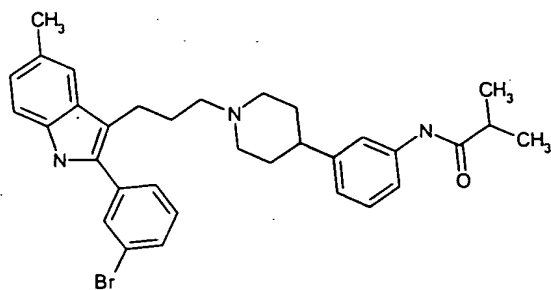
762

6.3



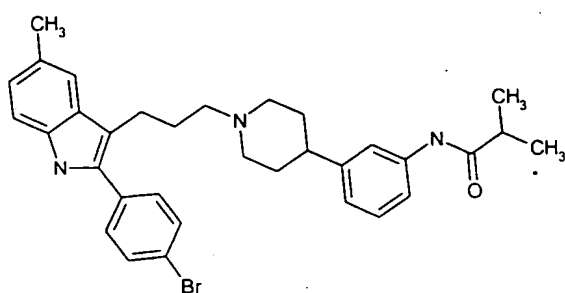
763

1.9



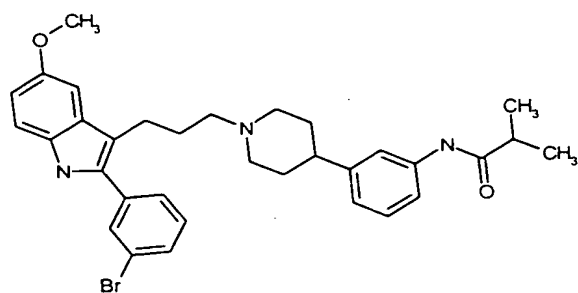
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14.6

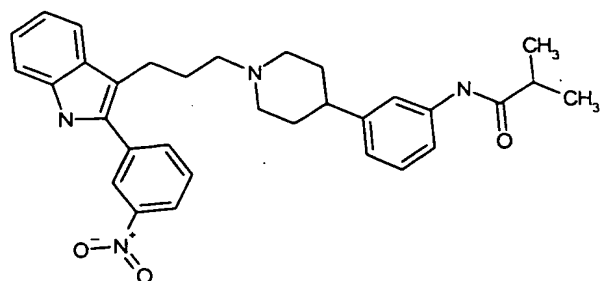


765

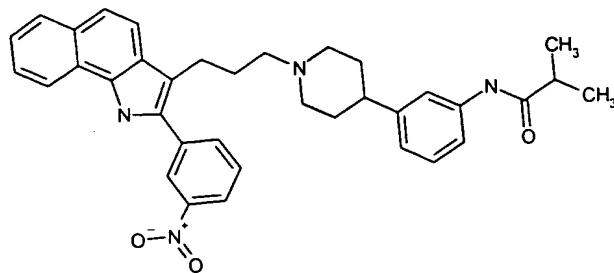
6.5



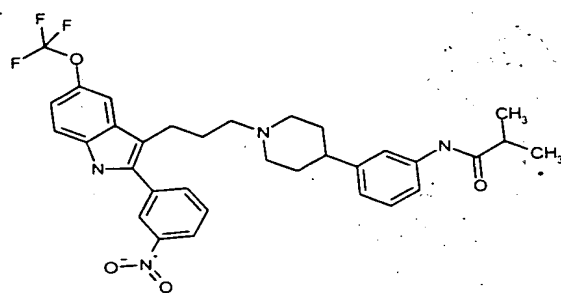
766 680 7.6



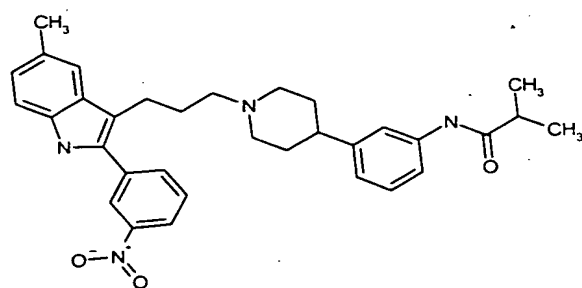
767 34.8



768 17.5



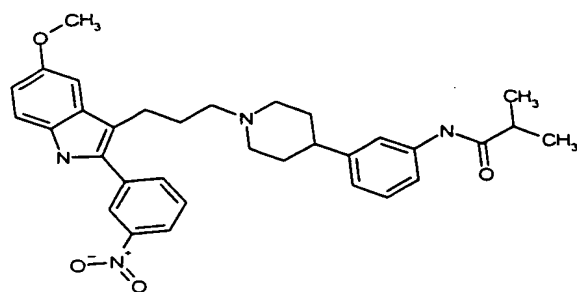
769 12.4



681

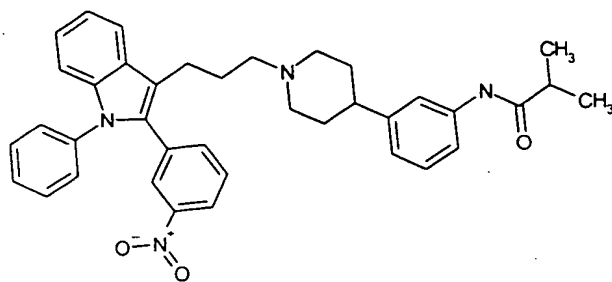
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12.7



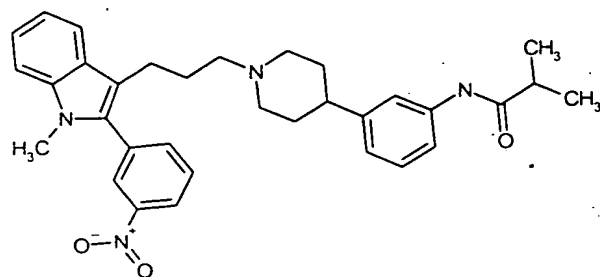
771

189.0



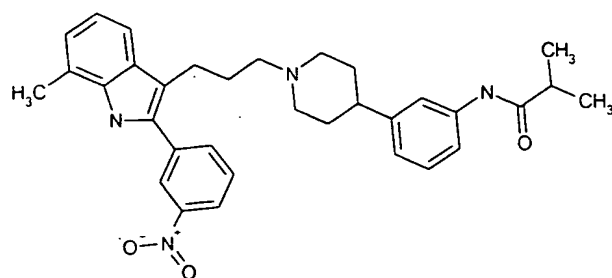
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14.9



773

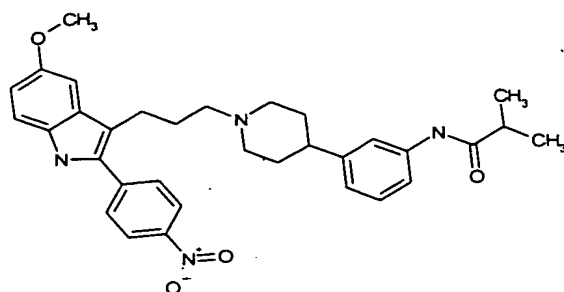
23.8



682

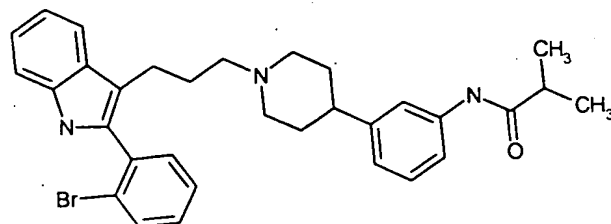
774

7.9



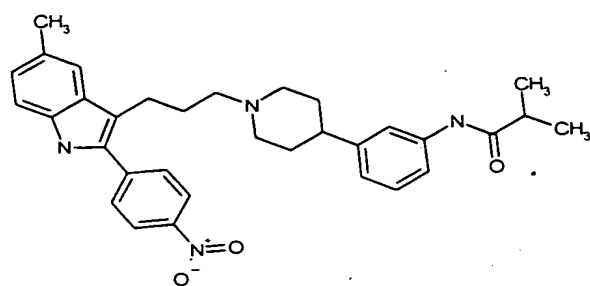
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4.9



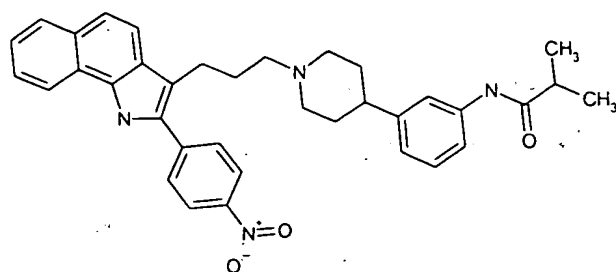
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18.2



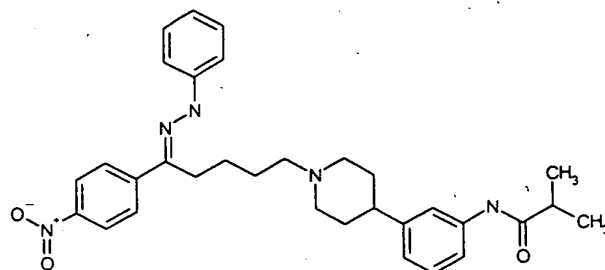
777

8.5



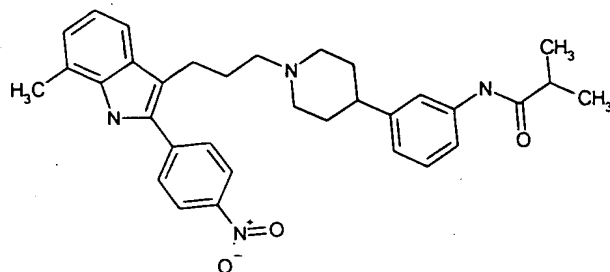
778

26.5



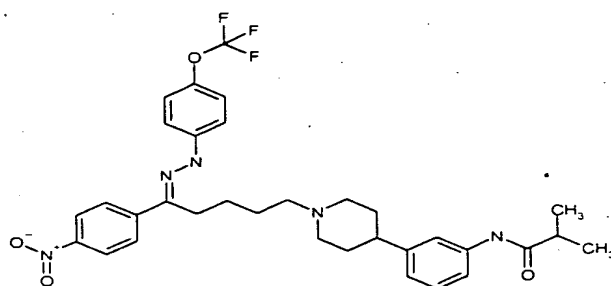
779

7.6



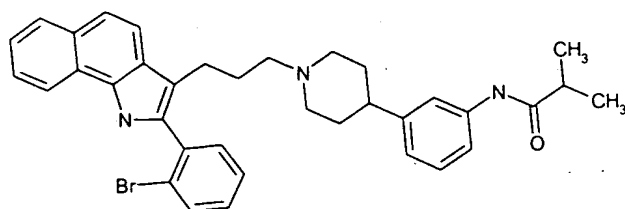
780

64.3



781

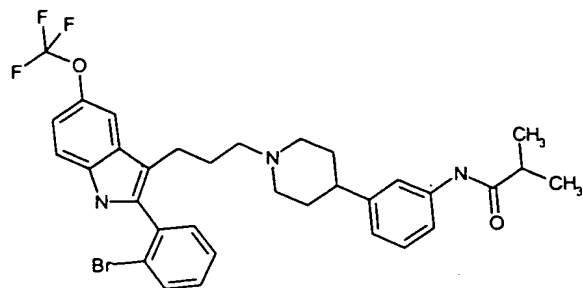
7.6



684

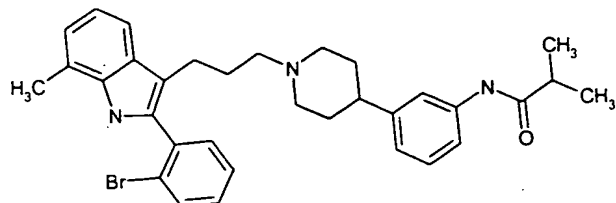
782

18.1



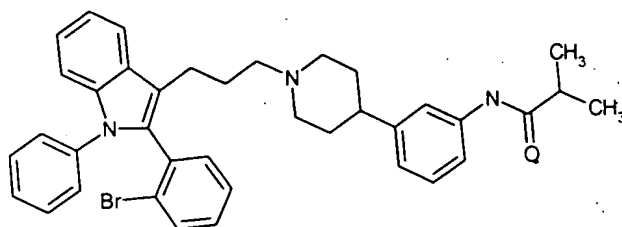
783

18.0



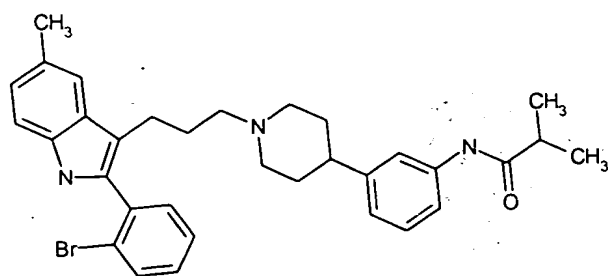
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121.2



785

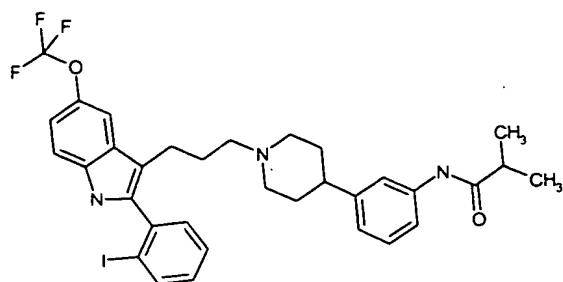
22.7



685

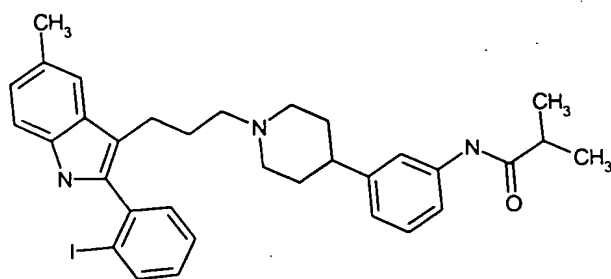
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19.7



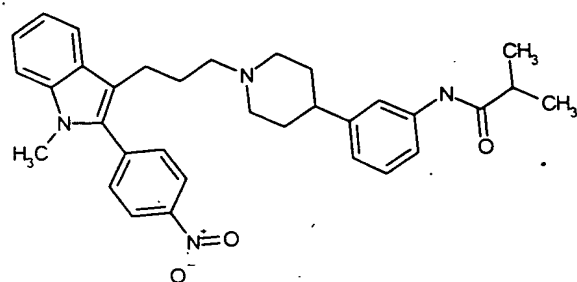
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21.6



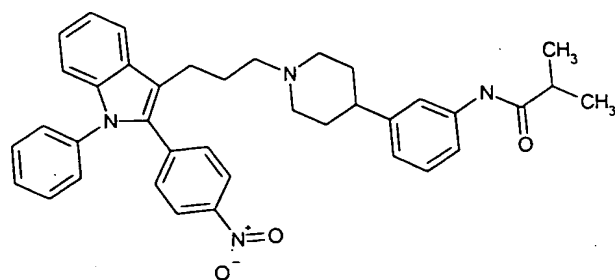
788

11.1



789

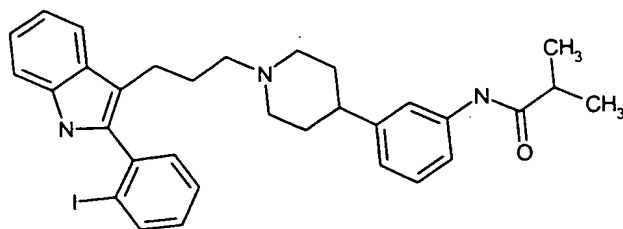
36.4



790

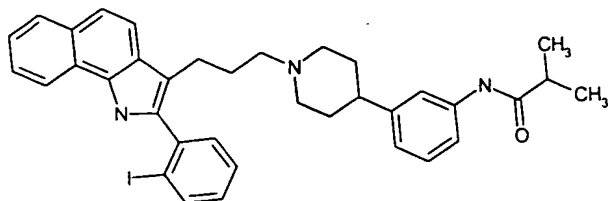
686

4.4



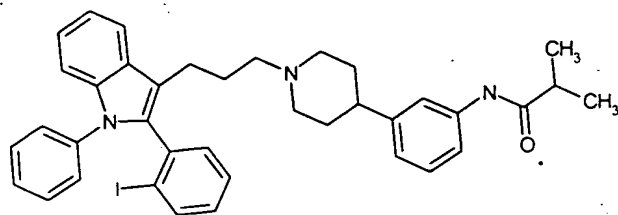
791

12.7



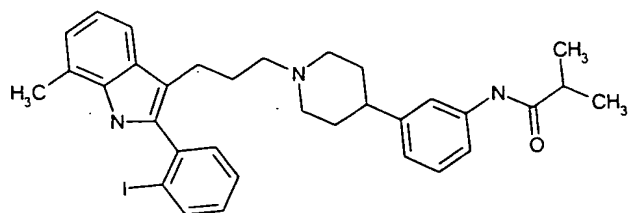
792

122.0



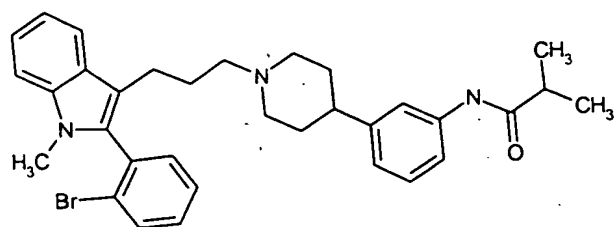
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16.3

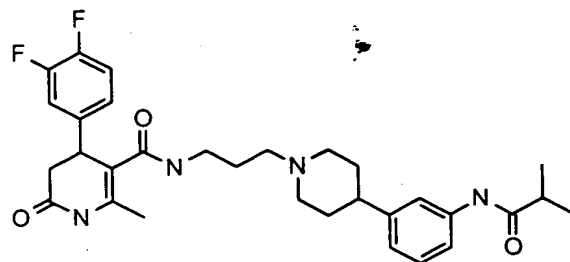




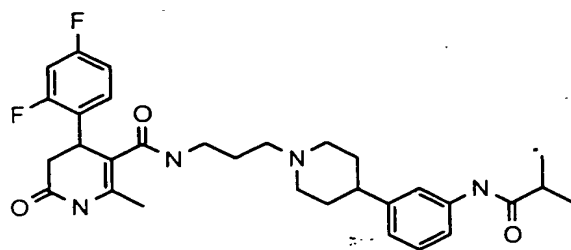
794 687 4.9



795 51.1



796 43.0



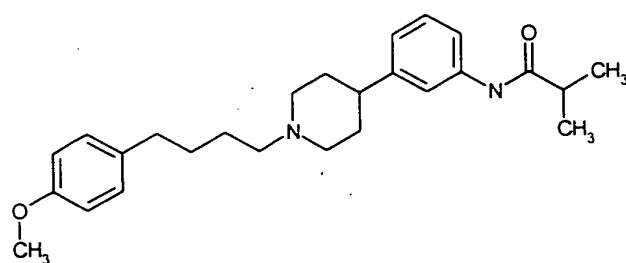
Example

Structure

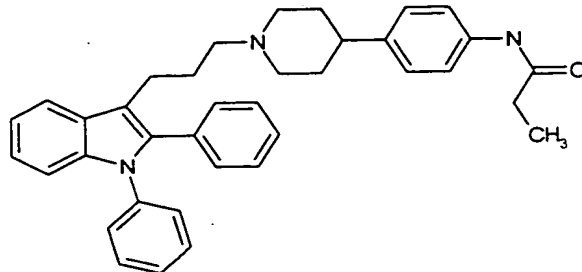
rMCH1  
Ki (nM)

797

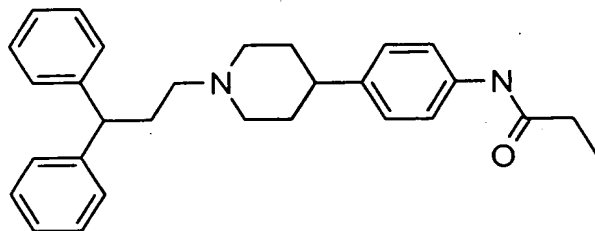
42.4



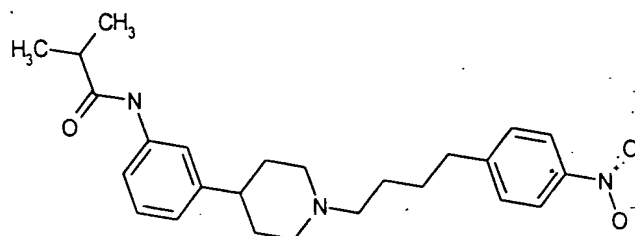
798 688 474.7



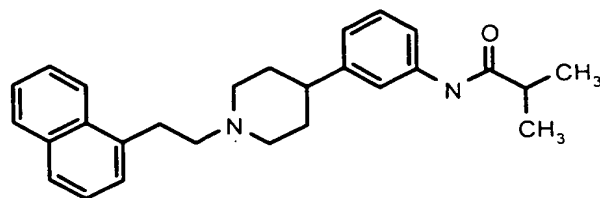
799 370.6



800 9.9



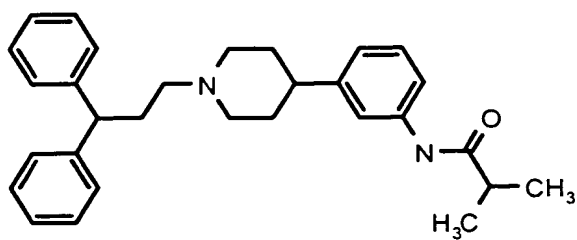
801 311.1



689

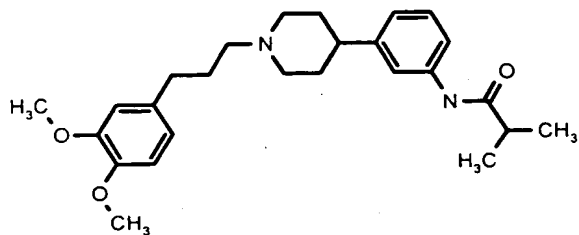
802

36.7



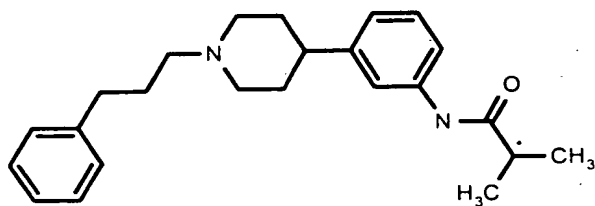
803

298.6



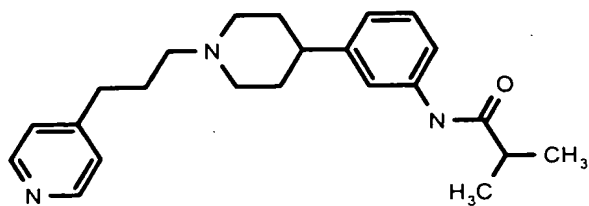
804

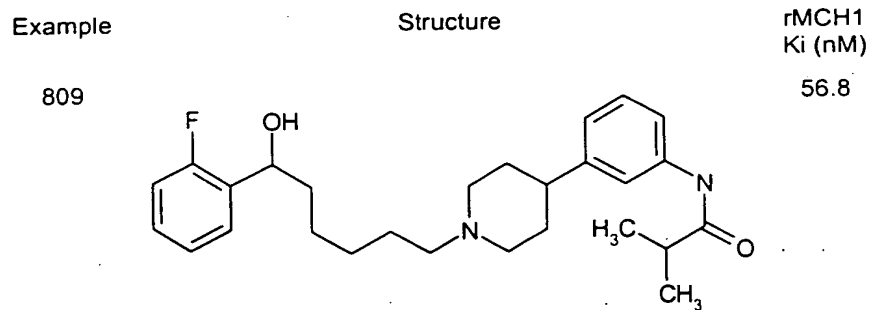
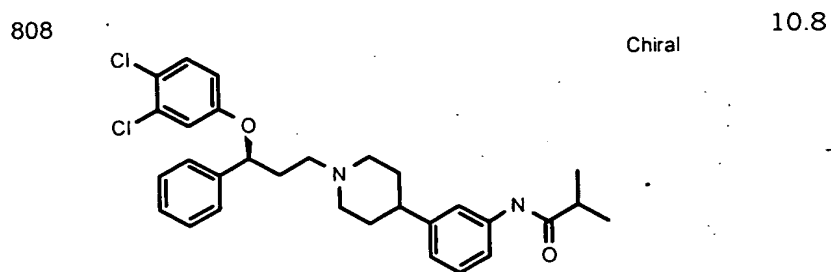
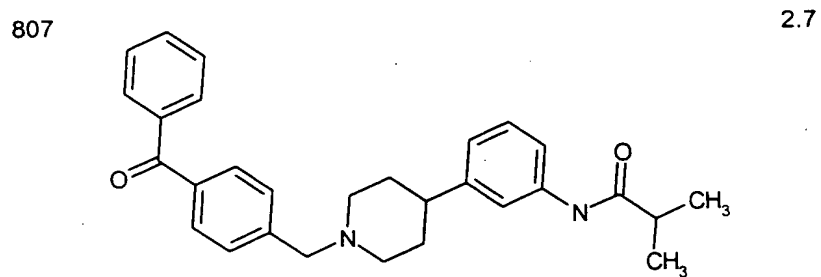
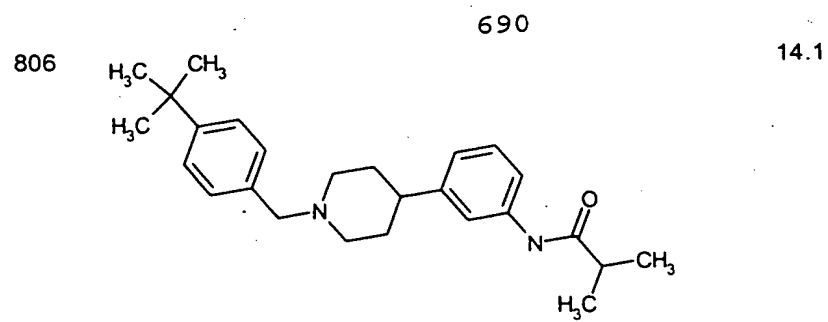
89.2



805

903.9

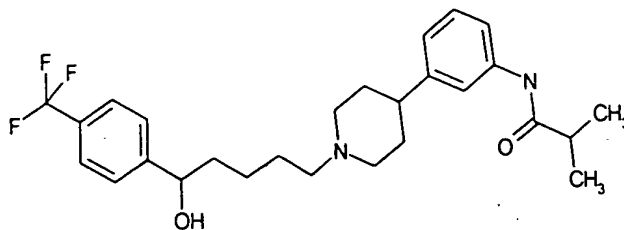




810

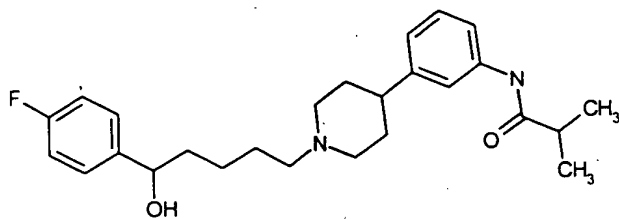
691

191.2



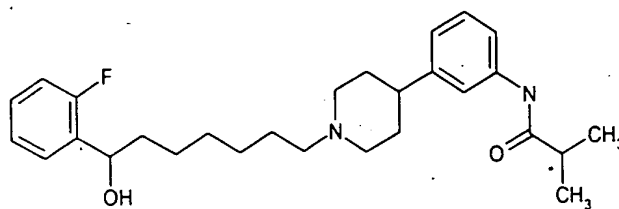
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190.8



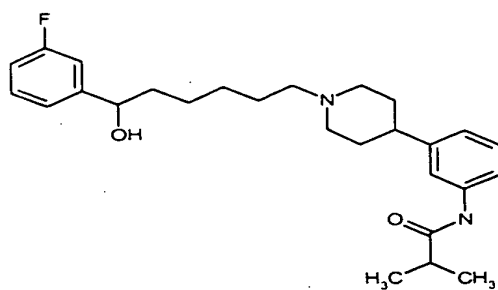
812

244.8



813

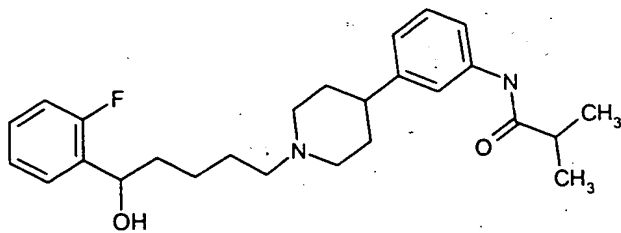
57.3



814

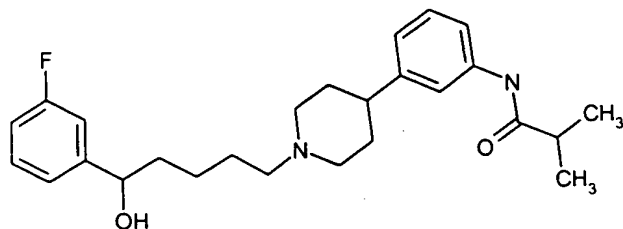
692

159.5



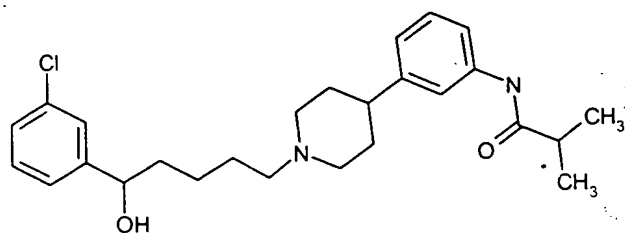
815

126.9



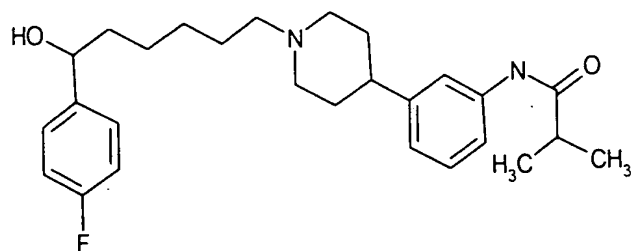
816

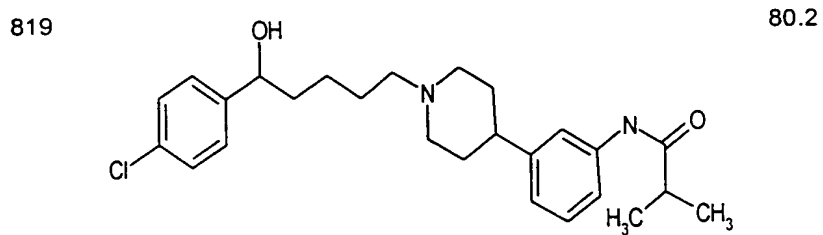
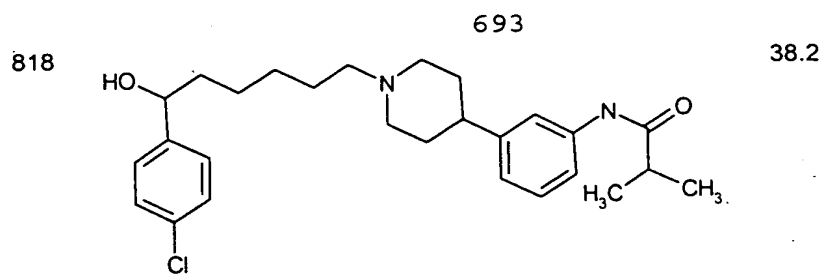
89.6



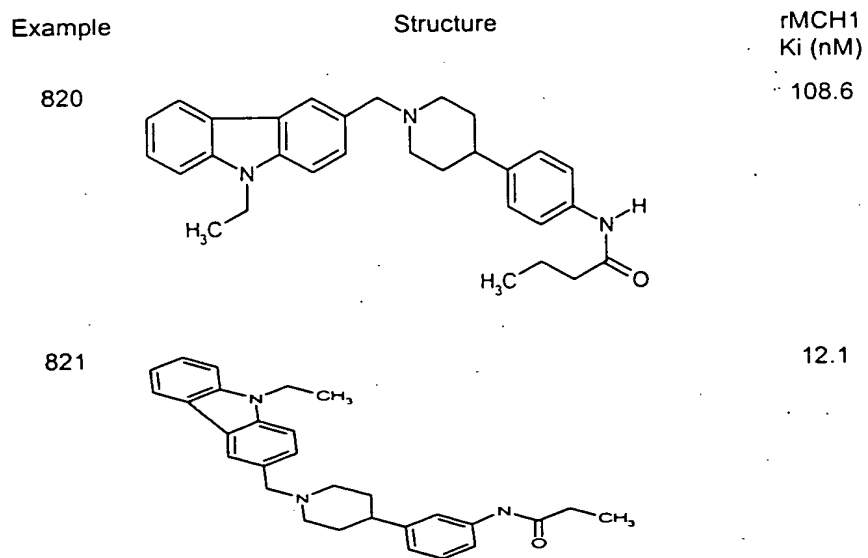
817

34.9

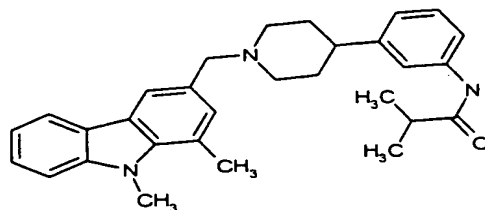




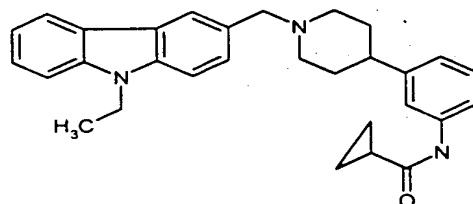
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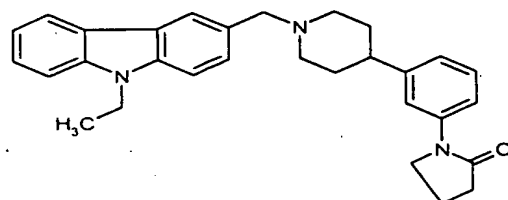
822 694 1.0



823 2.7



824 36.5



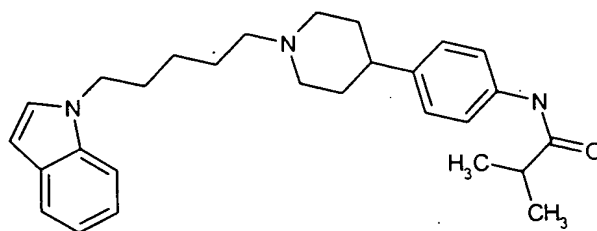
Example

Structure

rMCH1  
Ki (nM)

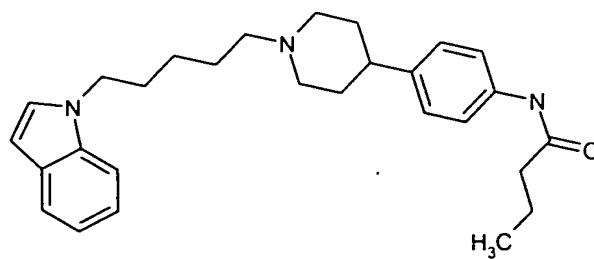
825

600.7



826

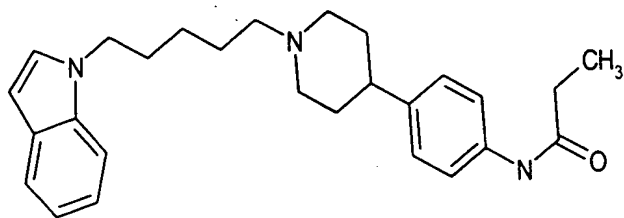
785.6





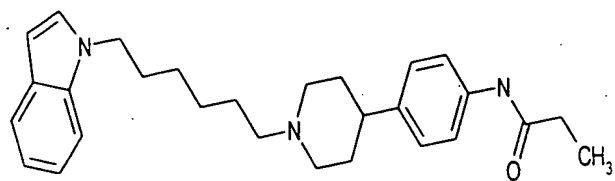
827

215.4



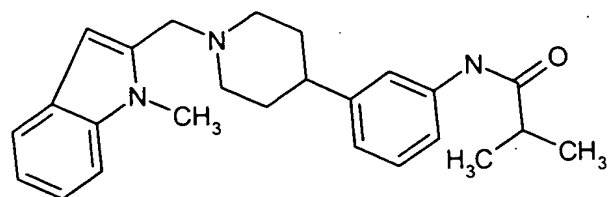
828

515.9



829

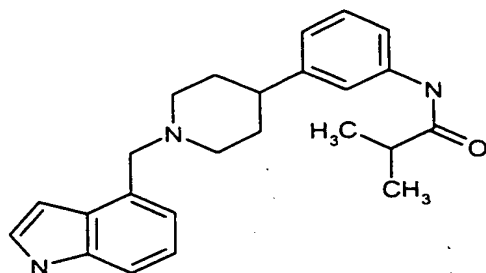
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830

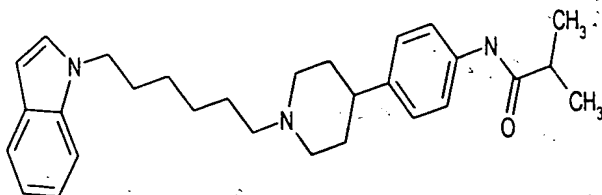
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468.6



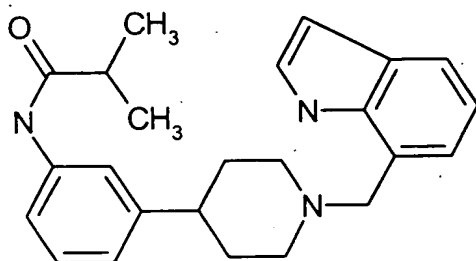
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569.8



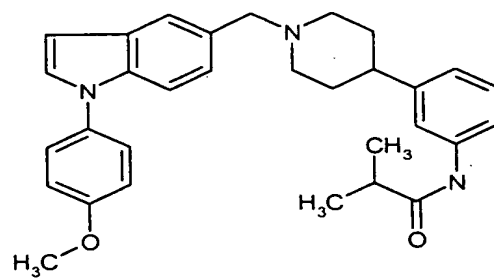
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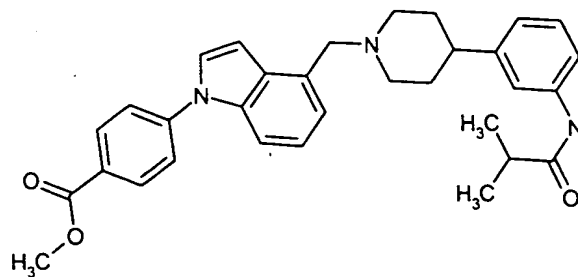


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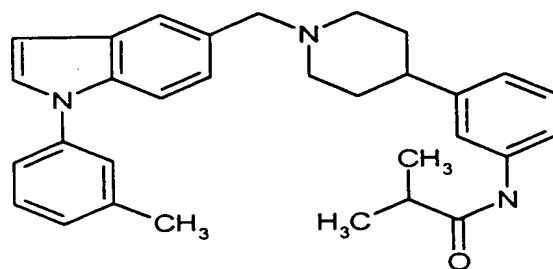
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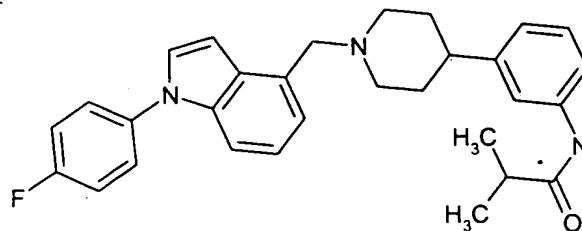
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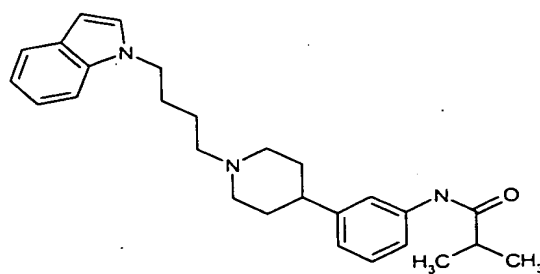
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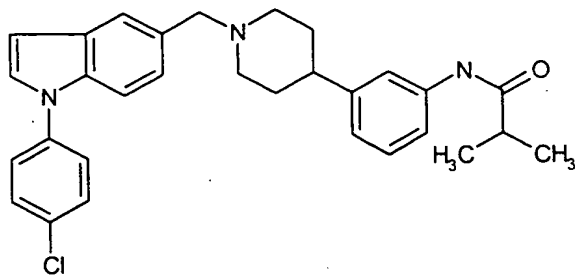
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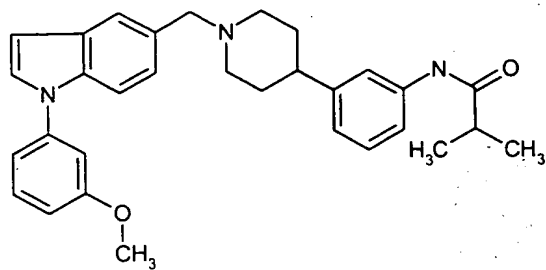
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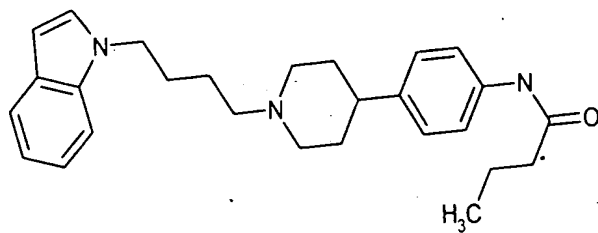
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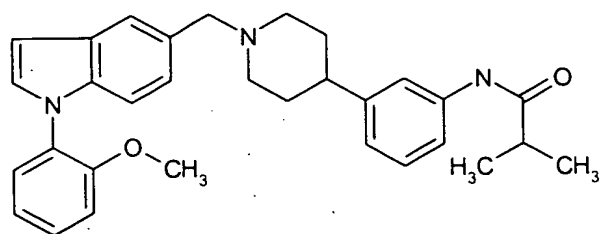
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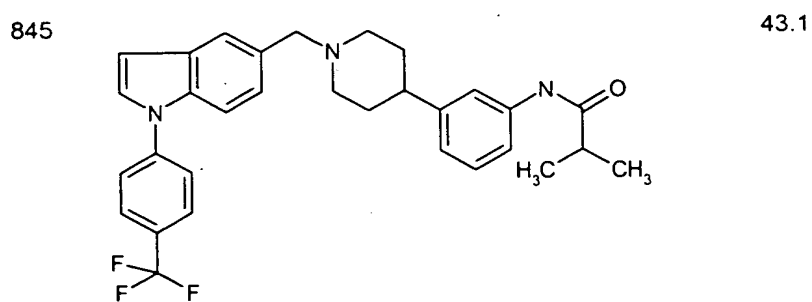
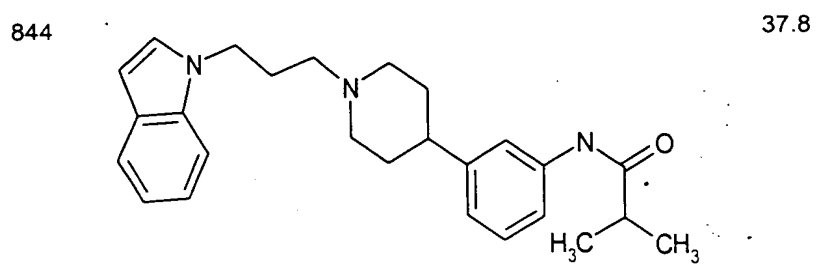
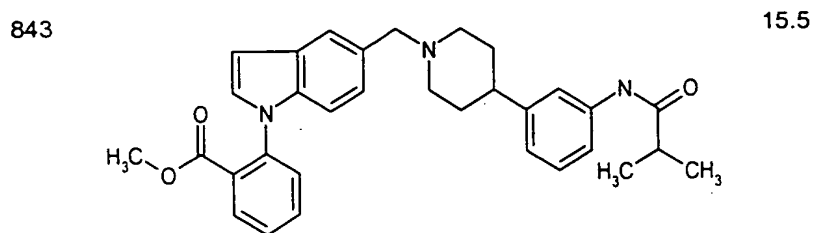
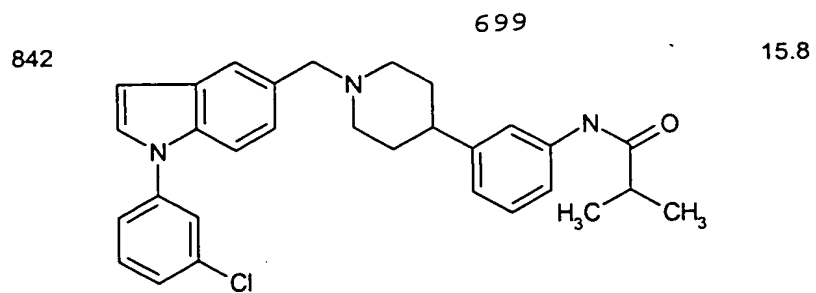


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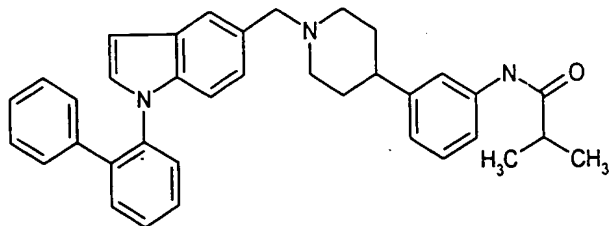


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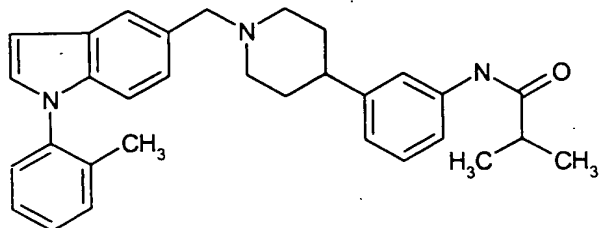




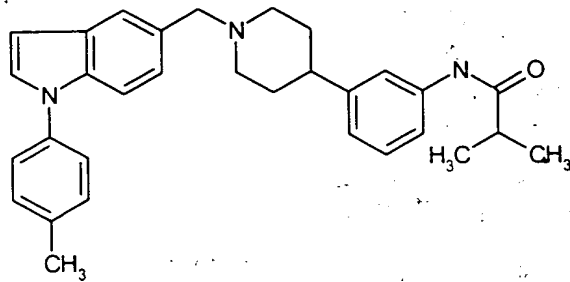
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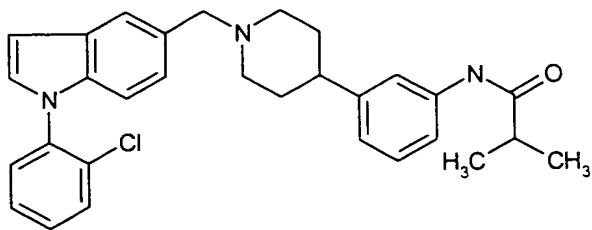
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848 19.1



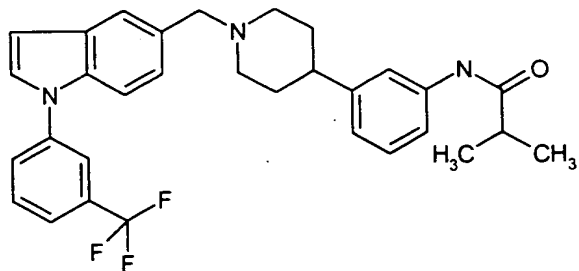
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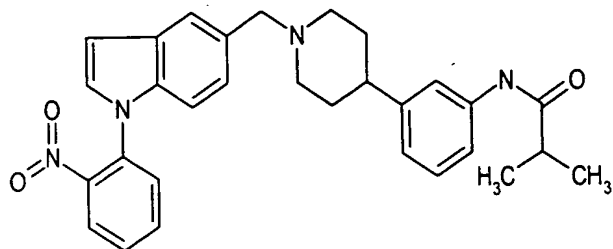
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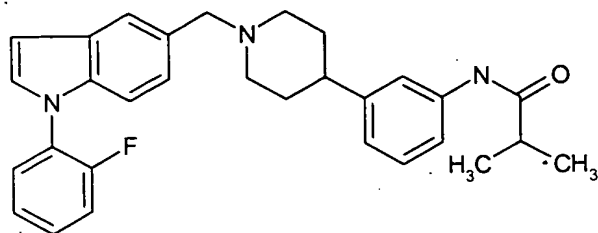
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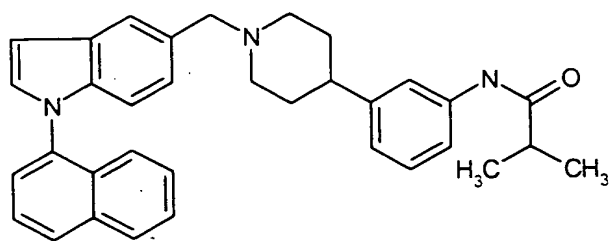
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14.5

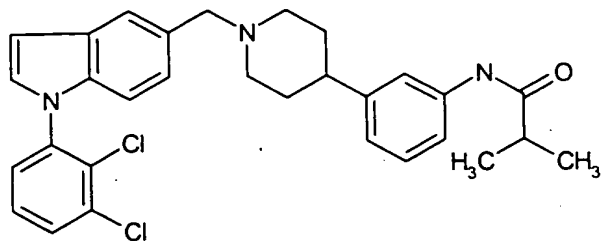


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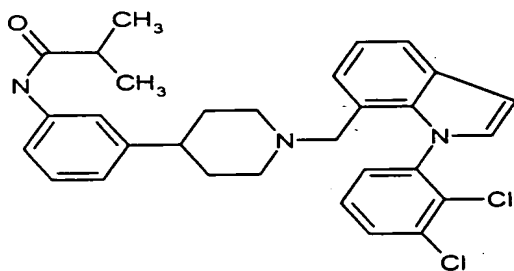
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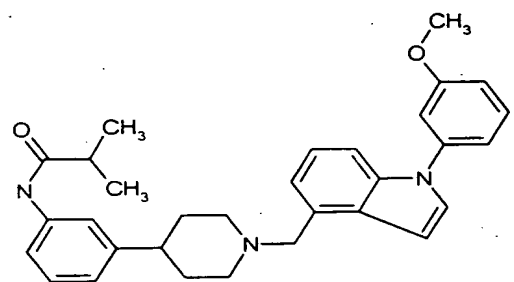
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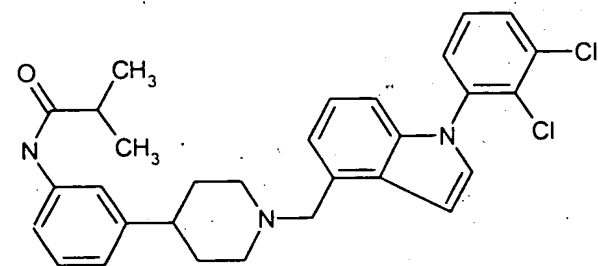
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856 122.6



857 89.8

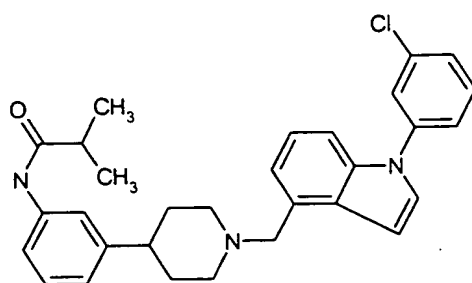




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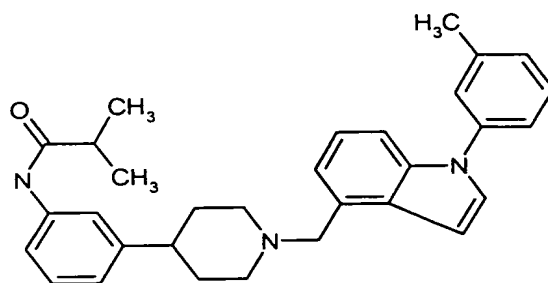
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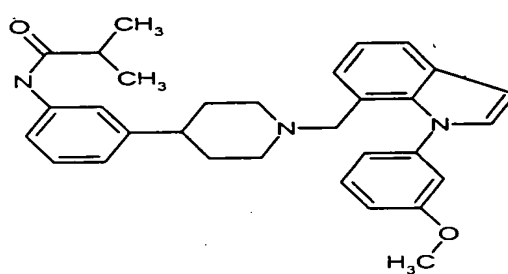
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320.7



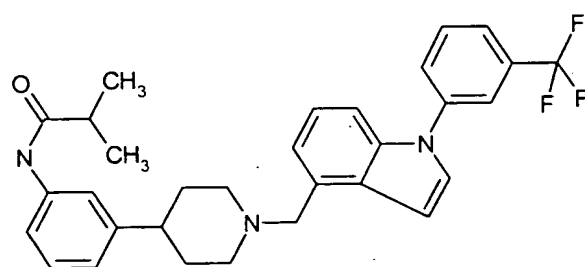
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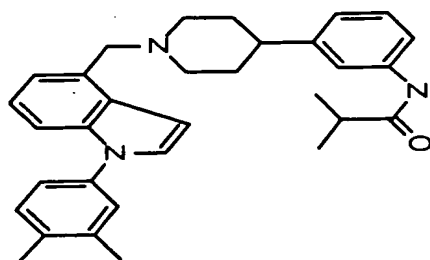


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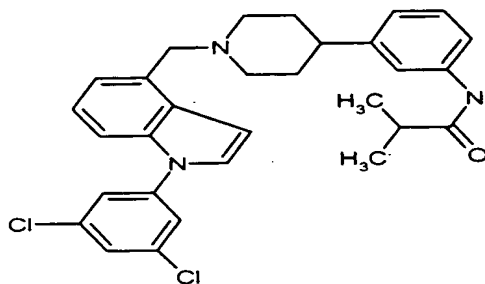
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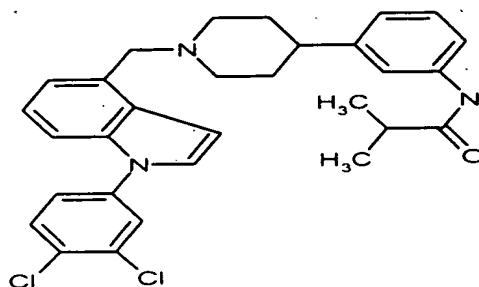
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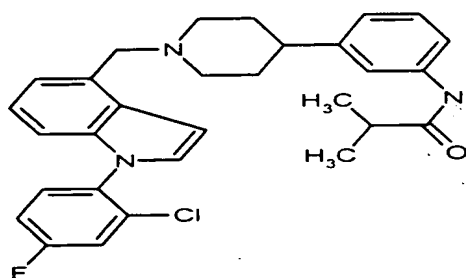
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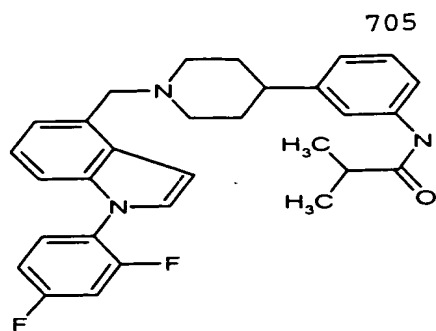
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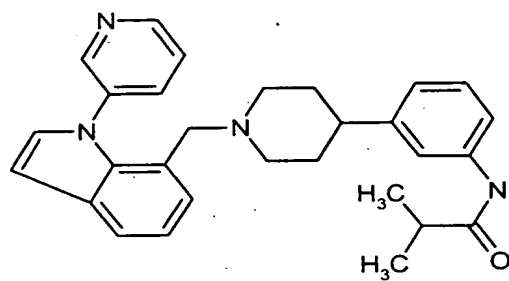


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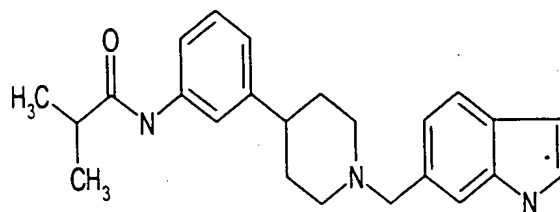
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867



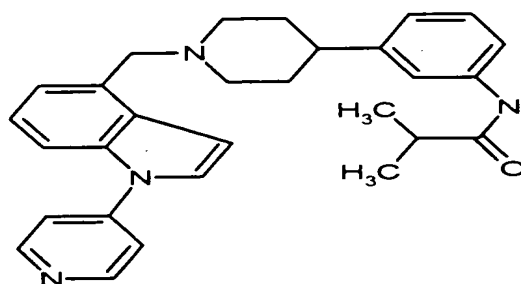
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868



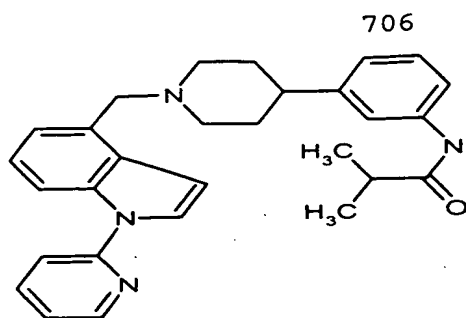
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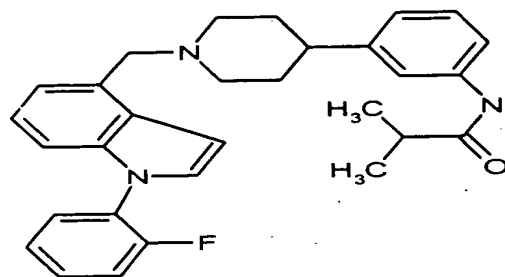
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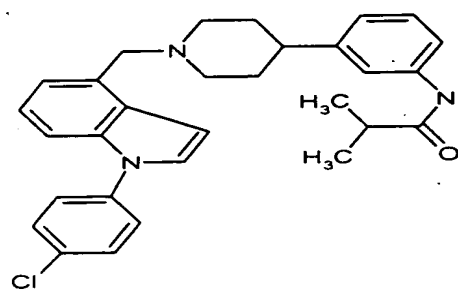
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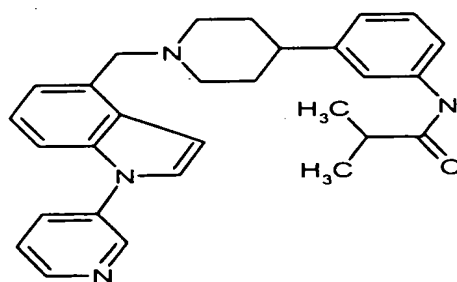
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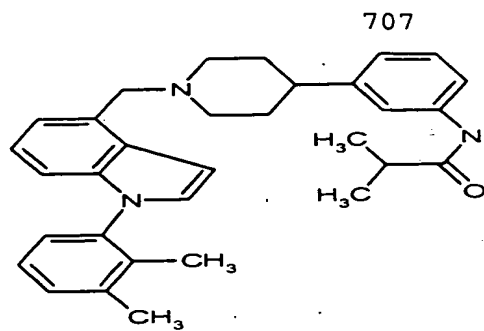
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873



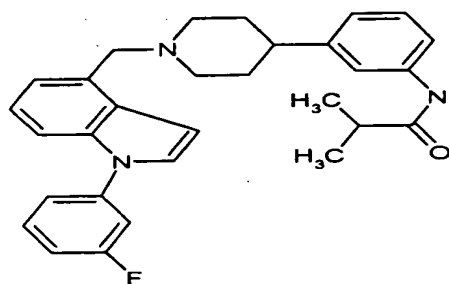
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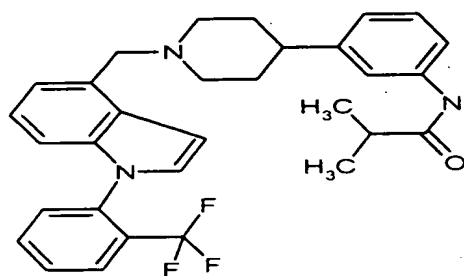
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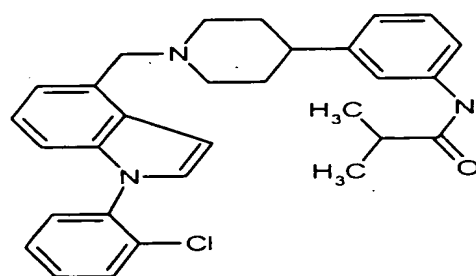
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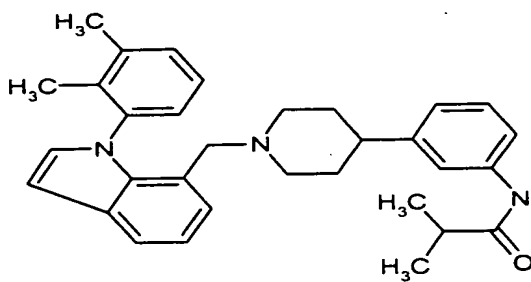
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877



245.1

878



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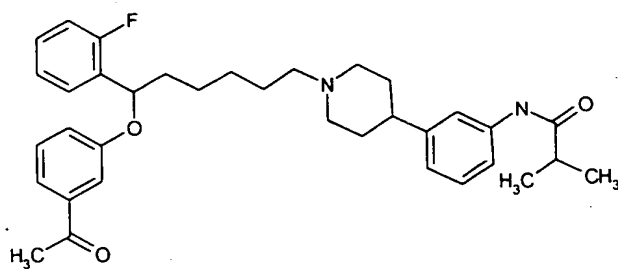
168.8

Example

Structure

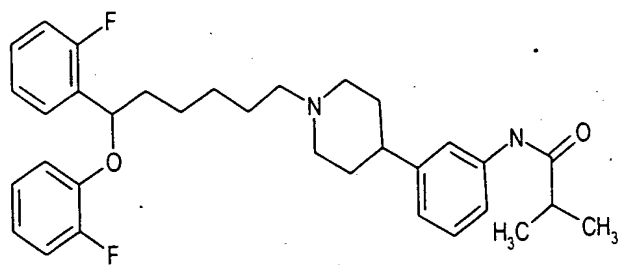
rMCH1  
Ki (nM)

888



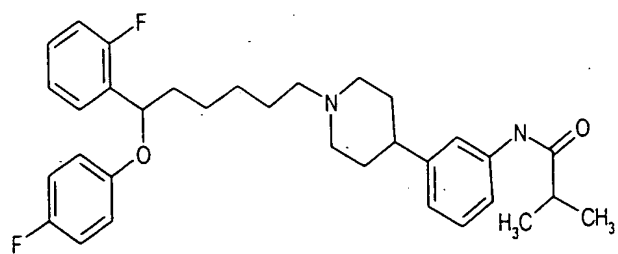
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889



8.6

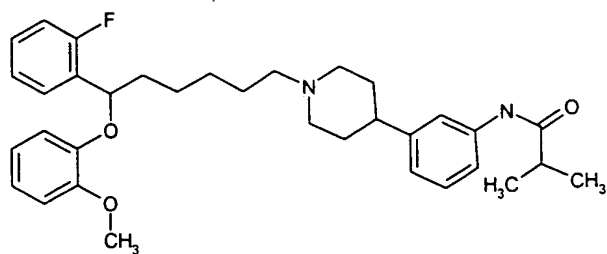
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11.1

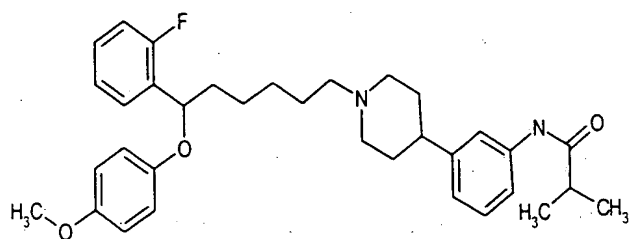
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6.5



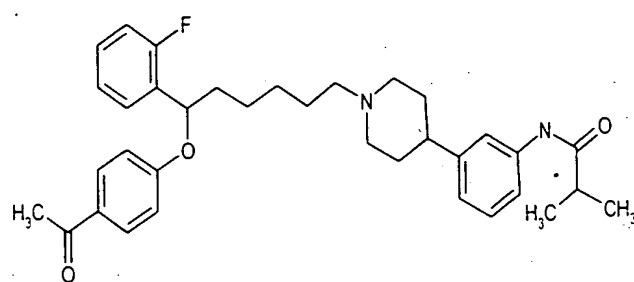
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17.3



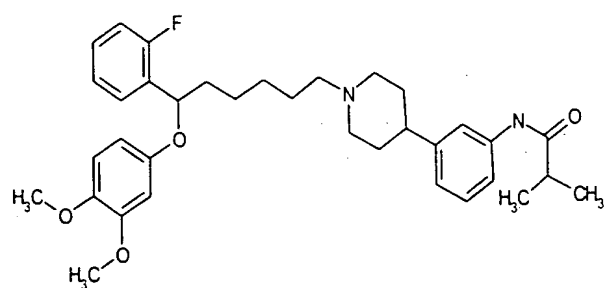
893

23.0



894

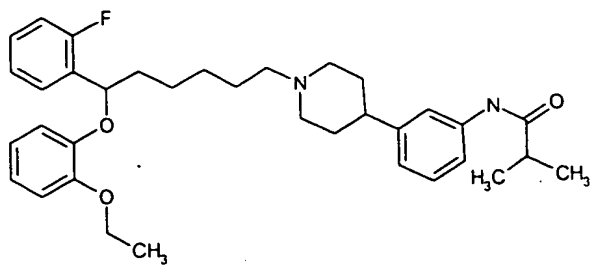
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710

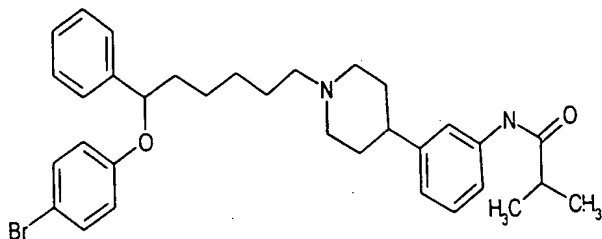
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6.4



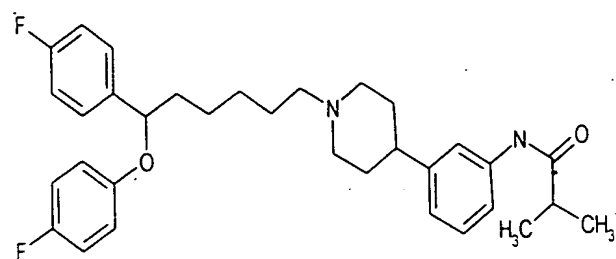
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30.3



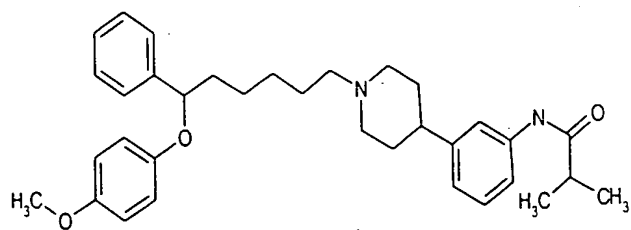
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6.4



898

33.7

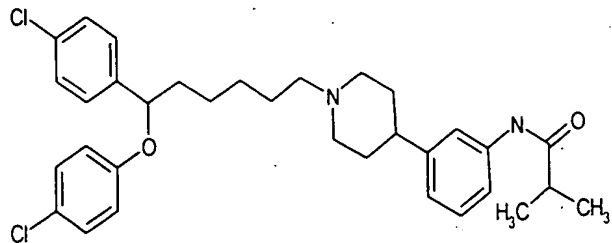




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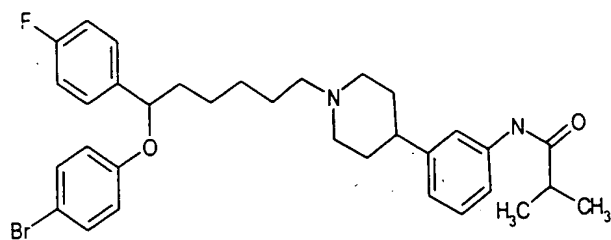
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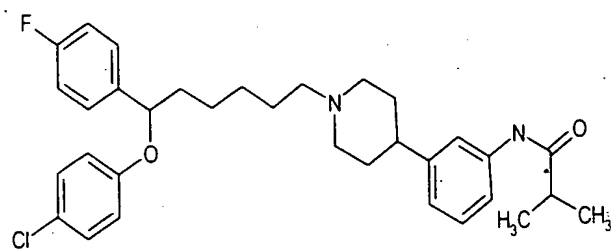
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11.2



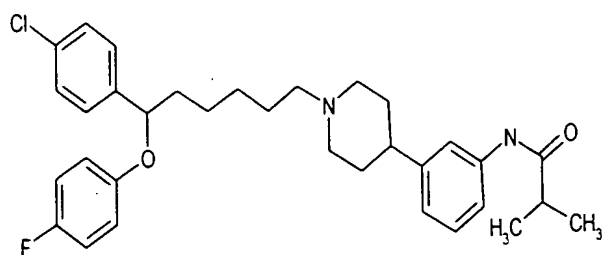
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8.2



902

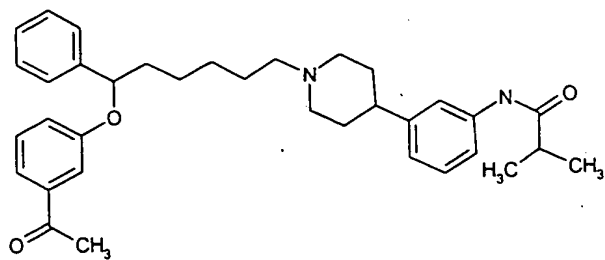
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712

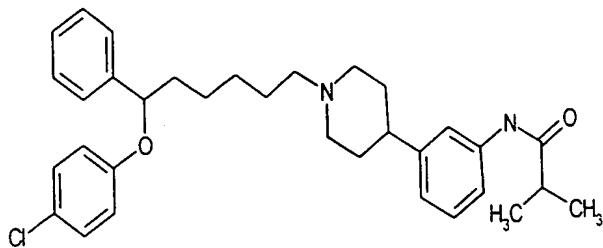
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12.2



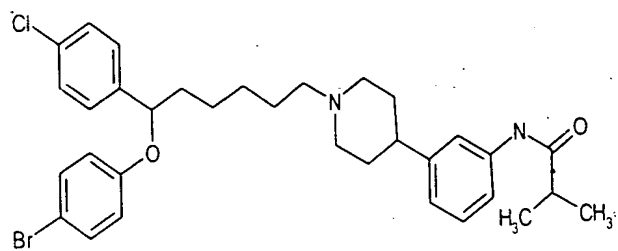
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14.2



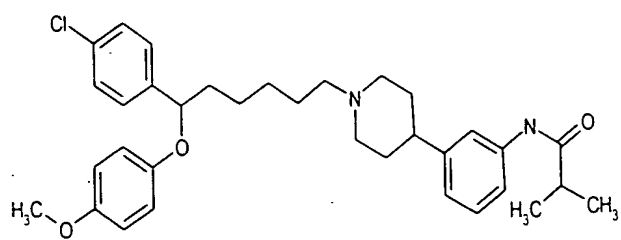
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5.9



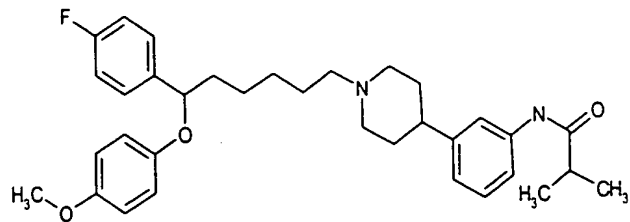
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5.7



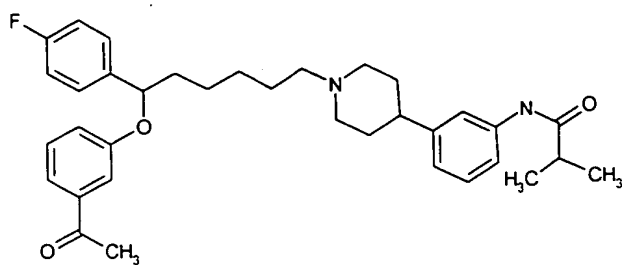
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3.1



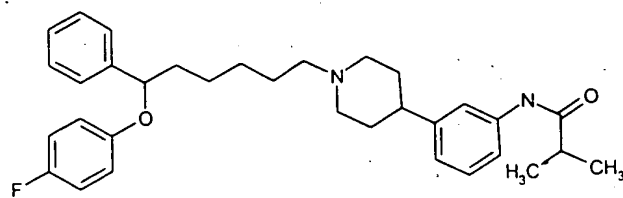
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3.7



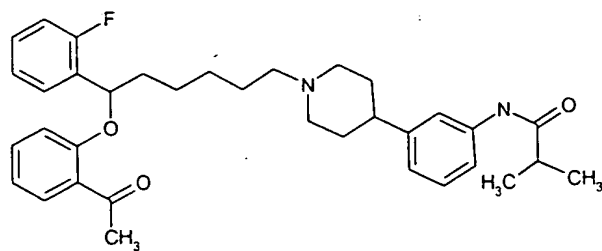
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10.0



910

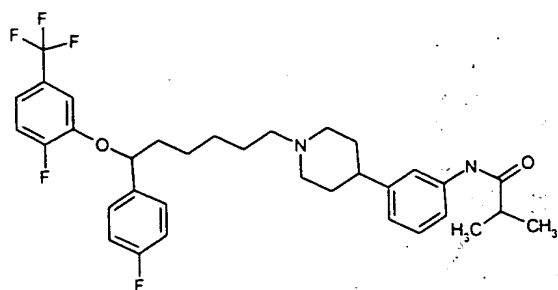
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714

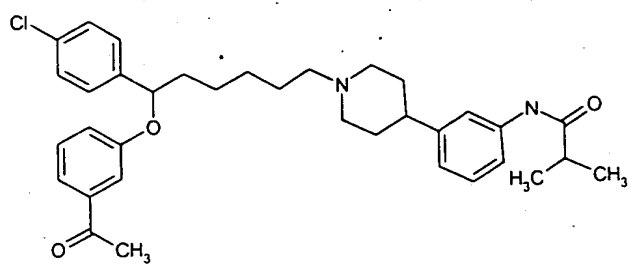
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7.6



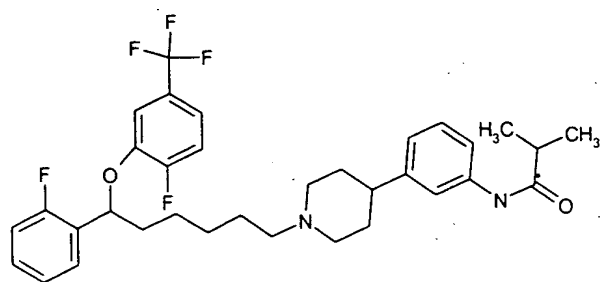
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5.7



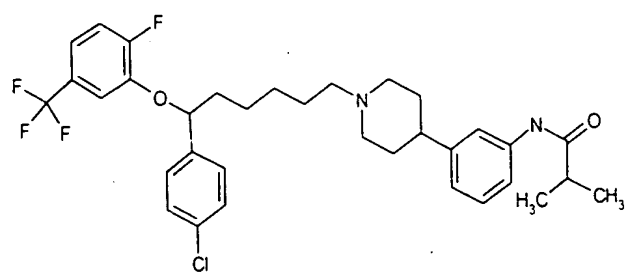
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12.9



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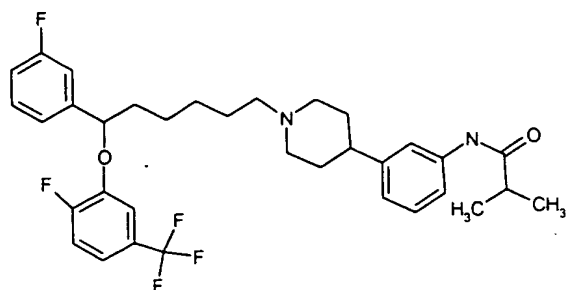
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715

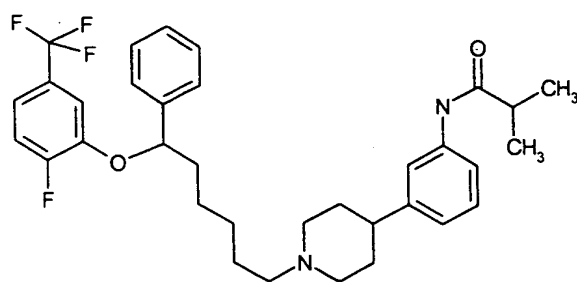
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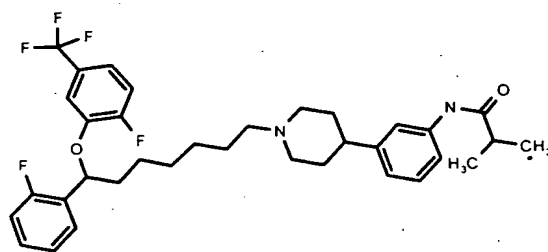
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20.2



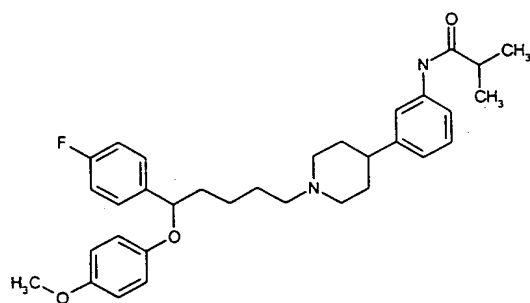
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78.0



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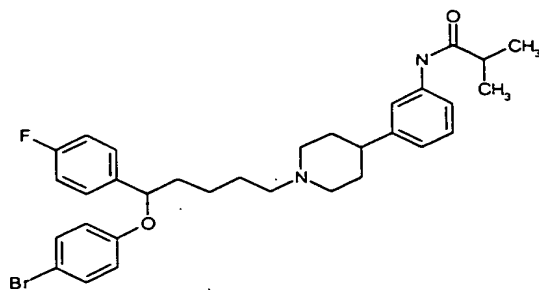
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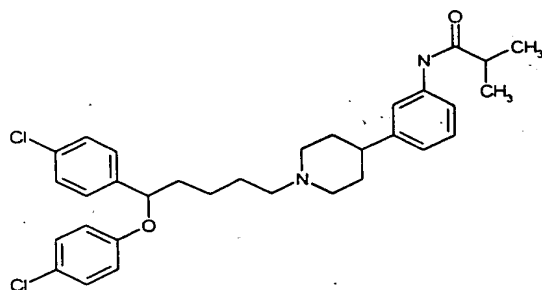
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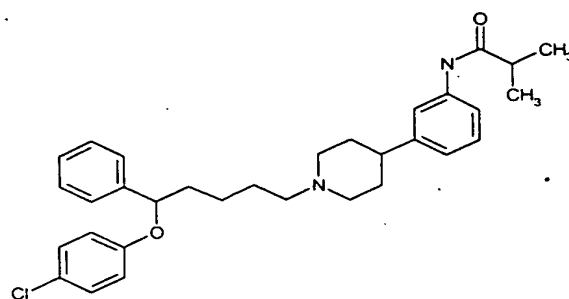
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6.9



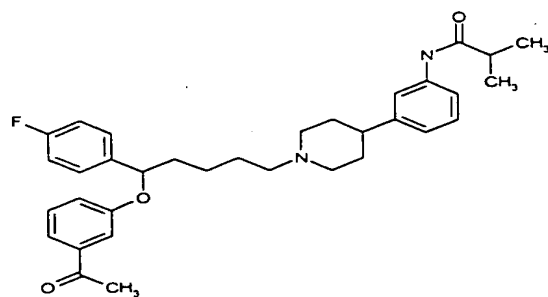
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6.8



922

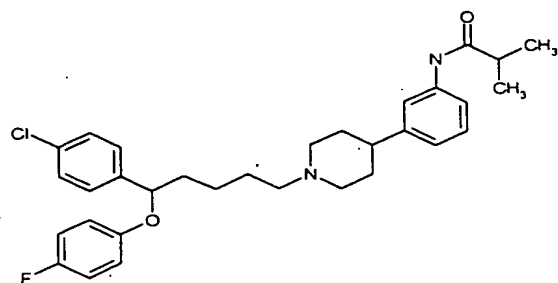
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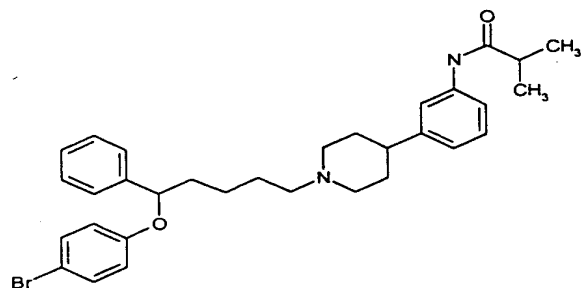
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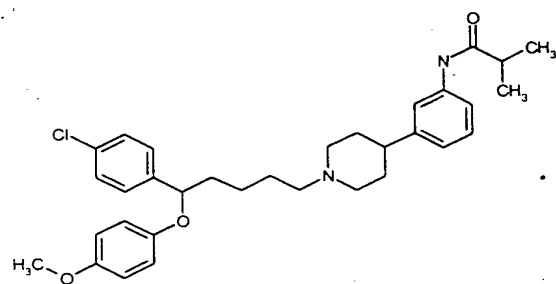
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13.1



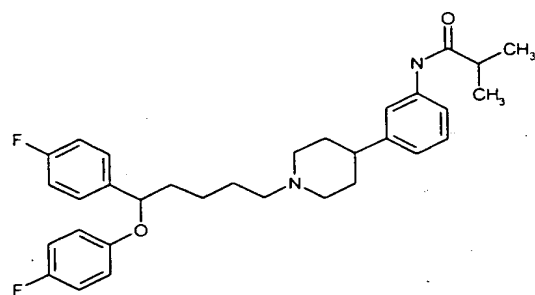
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13.4



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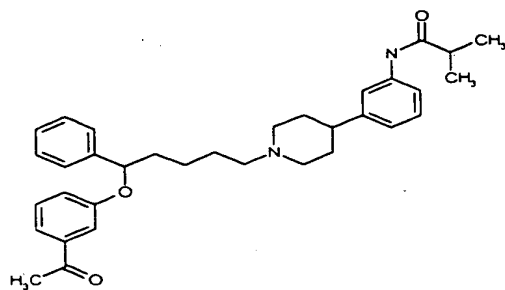
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927

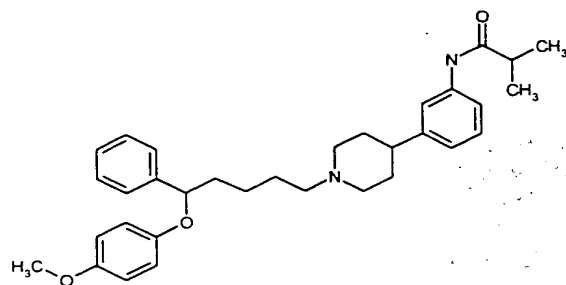
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60.7



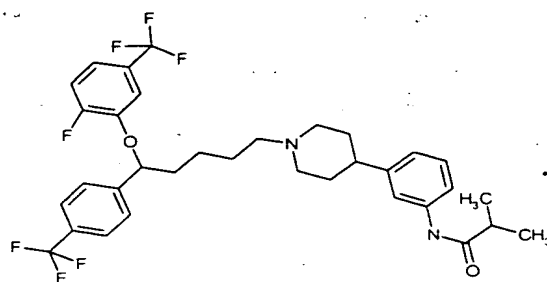
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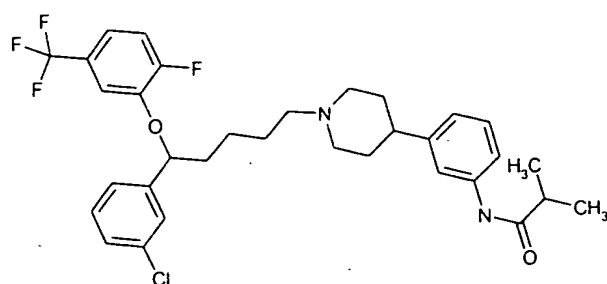
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29.9



930

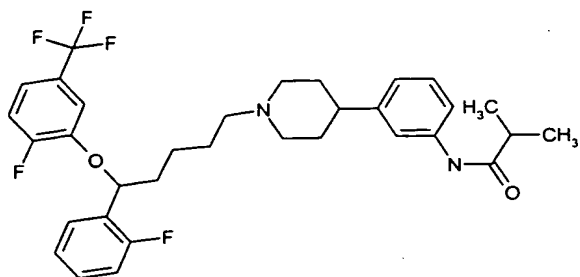
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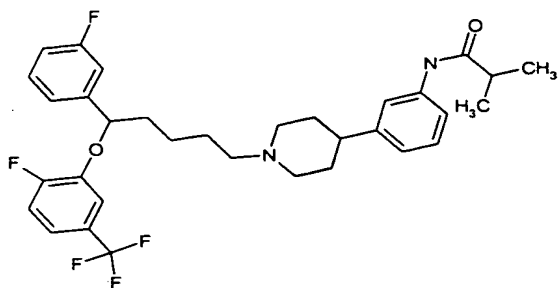
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9.6



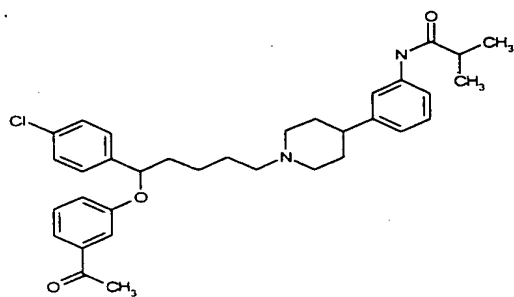
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9.4



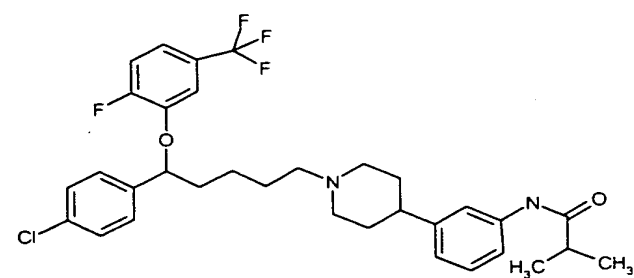
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10.9



934

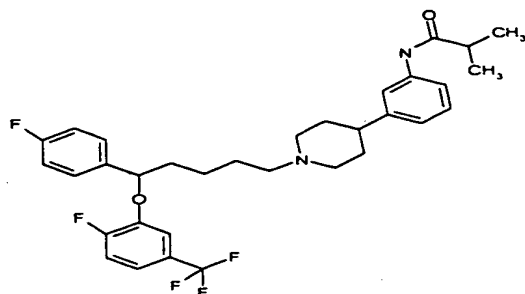
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935

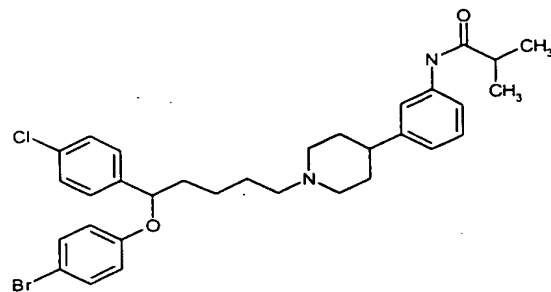
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19.7



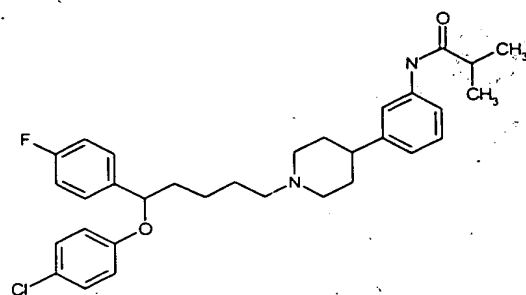
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11.6



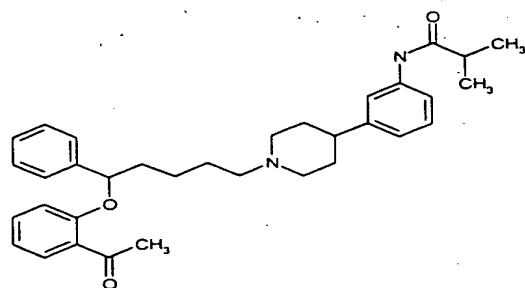
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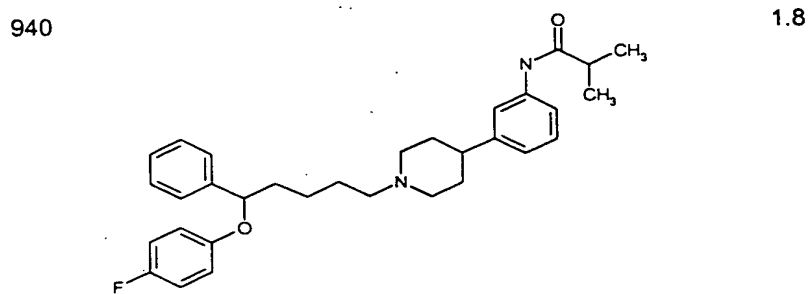
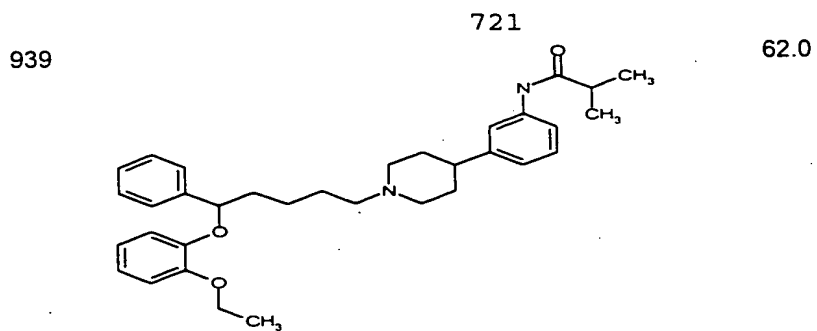
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938

608.6





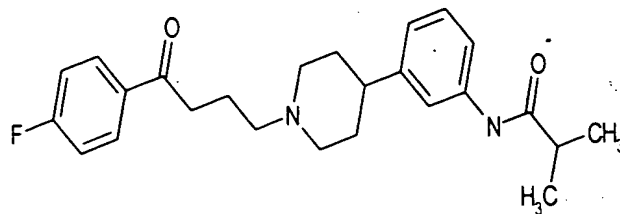
Example

Structure

rMCH1  
Ki (nM)

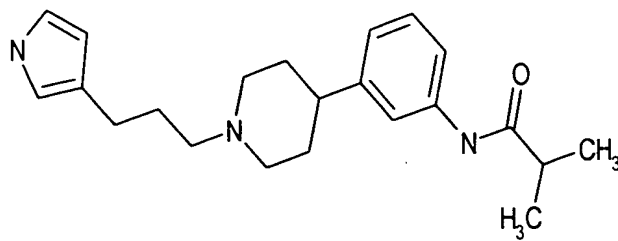
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15.2



942

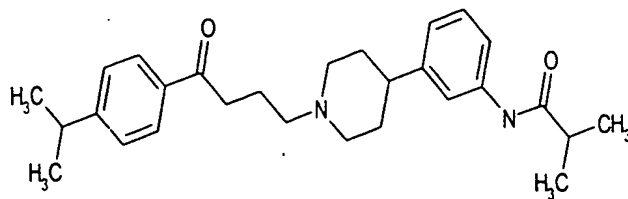
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943

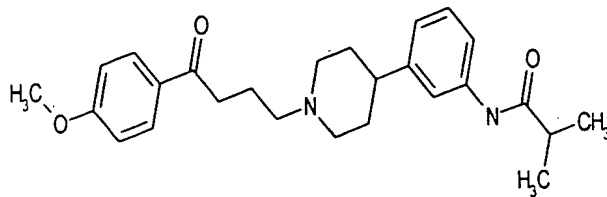
722

101.7



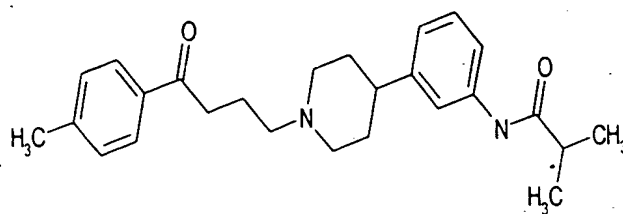
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38.8



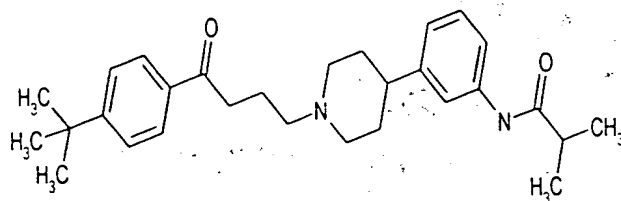
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31.2



946

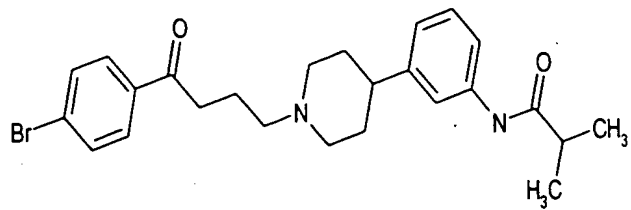
336.6



947

723

4.3



948

21.2

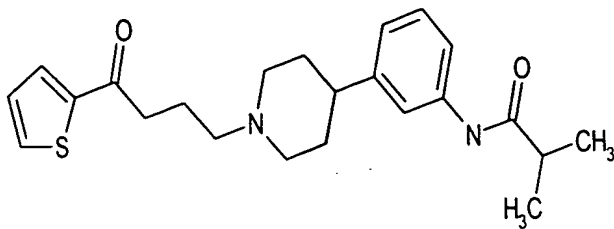


Table 2: Binding affinities (K<sub>i</sub>) at the rat MCH<sub>1</sub>, human Dopamine D<sub>2</sub>, human Histamine H<sub>1</sub> and human Alpha-1a Adrenergic receptors.

Compound	rMCH <sub>1</sub> K <sub>i</sub> (nM)	hD <sub>2</sub> K <sub>i</sub> (nM)	hH <sub>1</sub> K <sub>i</sub> (nM)	hAlpha-1a K <sub>i</sub> (nM)
1	90	6092	823	49
2	3.9	2839	700	32.1
3	768	ND	ND	ND
4	357	ND	ND	ND
5	14.2	1139	1618	9.1
6	274	ND	ND	ND
7	1000	ND	ND	ND
8	627	ND	ND	ND
9	69	1430	1733	26.4
10	2.8	862	461	19.4
11	197	ND	ND	ND
12	84	771	571	57
13	11.9	551	ND	61
14	167	ND	ND	ND
15	720	ND	ND	ND
16	272	ND	ND	ND
17	342	ND	ND	ND
18	29.5	782	ND	115
19	506	ND	ND	ND
20	21	470	ND	41.3
21	630	ND	ND	ND

Table 2: Binding affinities (Ki) at the rat MCH1, human Dopamine D2, human Histamine H1 and human Alpha-1a Adrenergic receptors.

22	52	5181	2277	284
23	1036	ND	ND	ND
24	67	1252	ND	127
25	463	ND	ND	ND
26	192	1977	ND	516
27	91	503	ND	130
28	511	ND	ND	ND
29	654	ND	ND	ND
30	382	ND	ND	ND
31	362	ND	ND	ND
32	160	ND	ND	ND
33	615	ND	ND	ND
34	651	ND	ND	ND
35	11.5	9654	2000	533
36	62	12,026	2454	1489
37	29.1	34,993	16,734	1087
38	18.2	>50000	6595	1592
39	11.8	>50000	6401	2937
40	50	7451	273	12.3
41	946	ND	ND	ND
42	118	ND	ND	ND
43	12	10,428	2560	434
44	11.5	8673	11,092	704

Table 2: Binding affinities (K<sub>i</sub>) at the rat MCH1, human Dopamine D2, human Histamine H1 and human Alpha-1a Adrenergic receptors.

45	1.6	42.2	3.4	18
46	187	ND	ND	ND
47	52	>50000	36,907	>50000
48	6.7	735	6390	452
49	7.1	471	39.1	140
50	3.9	1077	304	161
51	3.1	152	130	33.5
52	3.8	244	264	13.2
53	7.1	191	1320	221
54	4.9	83	283	187
55	5	162	1100	125
56	22.3	435	32.5	55
57	16.6	41,994	48,658	3206
58	20.1	390	590	233
59	12.9	262	46.9	49.1
60	0.923	52	546	22.3
61	13.6	281	969	310
62	12.8	319	25,320	719
63	22.4	766	25,307	1058
64	14.8	313	6994	1142
65	17	331	9390	1720
66	3.3	132	3473	944
67	5.9	133	2146	511



Table 2: Binding affinities (K<sub>i</sub>) at the rat MCH1, human Dopamine D2, human Histamine H1 and human Alpha-1a Adrenergic receptors.

68	9.3	66	329	204
69	32.5	46.6	>50000	232
70	50	1050	7998	1521
71	6.6	119	1710	226
72	31.4	41,454	33,096	645
73	22.3	41,454	6522	381
74	48.6	39,511	1862	333
75	11.8	19,041	2844	2469
76	44.6	41,454	39,710	10,965
77	25.7	447	4178	167
78	22.2	37.6	>50000	1313
79	19.4	244	507	722
80	14.3	833	9789	620
81	377	ND	ND	ND
82	11.2	ND	ND	ND
83	48.1	ND	ND	ND
84	121	ND	ND	ND
85	3.2	2449	3816	3021

## V. Synthesis of Compound A

Described below is the synthesis of Compound A.  
 5 Compound A is the radiolabeled compound that was used in  
 the radioligand binding assays described above.

### **N-[3-(1,2,3,6-TETRAHYDRO-4-PYRIDINYL)PHENYL]ACETAMIDE:**

The reaction of saturated of aqueous  $\text{Na}_2\text{CO}_3$  solution (25  
 10 mL), tert-butyl 4-[[trifluoromethyl)sulfonyl]oxy]-  
 1,2,3,6-tetrahydro-1-pyridine-carboxylate (20 mmol), 3-  
 acetamidophenylboronic acid (30 mmol) and tetrakis-  
 triphenylphosphine palladium (0) (1.15 g) in  
 dimethoxyethane (40 mL) at reflux temperature overnight  
 15 gave tert-butyl 4-[3-(acetylamino)phenyl]-3,6-dihydro-  
 1(2H)-pyridinecarboxylate. Deprotection of the BOC group  
 using HCl in dioxane followed by basification (pH 11-12)  
 gave the desired product.

20 **TERT-BUTYL N-(3-BROMOPROPYL)CARBAMATE:** was prepared from  
 3-bromopropylamine hydrobromide and  $\text{BOC}_2\text{O}$  in the presence  
 of base in dichloromethane.

**N-{3-[1-(3-AMINOPROPYL)-1,2,3,6-TETRAHYDRO-4-  
 25 PYRIDINYL]PHENYL}ACETAMIDE:** The reaction of tert-butyl  
 N-(3-bromopropyl)carbamate and N-[3-(1,2,3,6-tetrahydro-  
 4-pyridinyl)phenyl]acetamide in refluxing dioxane with  
 catalytic  $\text{Bu}_4\text{NI}$  and base as described in Scheme A gave  
 tert-butyl 3-(4-[3-(acetylamino)phenyl]-3,6-dihydro-  
 30 1(2H)-pyridinyl)propylcarbamate. Deprotection of the  
 BOC group using HCl in dioxane followed by basification  
 (pH 11-12) gave the desired product.

METHYL (4S)-3-({[3-(4-[3-(ACETYLAMINO)PHENYL]-3,6-DIHYDRO-1(2H)-PYRIDINYL]PROPYL]AMINO}CARBONYL)-4-(3,4-DIFLUOROPHENYL)-6-(METHOXYMETHYL)-2-OXO-1,2,3,4-

TETRAHYDRO-5-PYRIMIDINECARBOXYLATE: Prepared from the

5 reaction of 5-methyl 1-(4-nitrophenyl) (6S)-6-(3,4-difluorophenyl)-4-(methoxymethyl)-2-oxo-3,6-dihydro-

1,5(2H)-pyrimidinedicarboxylate (describe in PCT Publication No. WO 00/37026, published June 29, 2000)

10 and N-{3-[1-(3-aminopropyl)-1,2,3,6-tetrahydro-4-pyridinyl]phenyl}acetamide: <sup>1</sup>H NMR δ 8.90 (t, 1 H, J=3.6 Hz), 7.75 (s, 1 H), 7.50-7.00 (m, 8 H), 6.68 (s, 1 H), 6.03 (br s, 1 H), 4.67 (s, 2 H), 3.71 (s, 3 H), 3.47 (s, 3 H), 3.38 (ABm, 2 H), 3.16 (m, 2 H), 2.71 (t, 2 H, J=5.4 Hz), 2.56 (m, 4 H), 2.35-1.90 (br, 2 H), 2.17 (s, 3 H), 1.82 (p, 2 H, J=7.2 Hz); ESMS, 612.25 (M+H)<sup>+</sup>.

TRITIATED METHYL (4S)-3-{{[3-{4-[3-(ACETYLAMINO)PHENYL]-1-PIPERIDINYL}PROPYL]AMINO}CARBONYL}-4-(3,4-DIFLUOROPHENYL)-6-(METHOXYMETHYL)-2-OXO-1,2,3,4-

20 TETRAHYDRO-5-PYRIMIDINECARBOXYLATE ([<sup>3</sup>H] COMPOUND A): This radiochemical synthesis was carried out by Amersham Pharmacia Biotech, Cardiff, Wales. A methanolic solution of methyl (4S)-3-({[3-(4-[3-

25 (acetylaminophenyl]-3,6-dihydro-1(2H)-pyridinyl]propyl]amino}carbonyl)-4-(3,4-difluorophenyl)-6-(methoxymethyl)-2-oxo-1,2,3,4-tetrahydro-5-

pyrimidinecarboxylate was exposed to tritium gas at 1 atmosphere pressure in the presence of 5% palladium on carbon with stirring overnight to give the tritiated

30 methyl (4S)-3-{{[3-{4-[3-(acetylaminophenyl]-1-piperidinyl}propyl]amino}carbonyl}-4-(3,4-difluorophenyl)-6-(methoxymethyl)-2-oxo-1,2,3,4-tetrahydro-5-pyrimidinecarboxylate ((+)-isomer) After

purification by reverse phase HPLC (Hypersil ODS, 4.6 x 100 mm, methanol:H<sub>2</sub>O:Et<sub>3</sub>N 10:90:1 to 100:0:1 in 15 min at 1.0 mL/min, with radiochemical and UV detection), this product was used as a radioligand in the MCH1 binding assays. The same procedure was carried out with H<sub>2</sub> gas in place of <sup>3</sup>H<sub>2</sub> to afford the non-radioactive version of Compound A.

## VI. In-Vivo Methods

10

The following *in vivo* methods were performed to predict the efficacy of MCH1 antagonists for the treatment of obesity (3-day body weight and sweetened condensed milk), depression (forced swim test), anxiety (social interaction test), and urinary disorders (DIRC and CSTI).

15

### Effects of MCH1 Antagonists on Body Weight (3 Day)

Male Long Evans rats (Charles River) weighing 180-200 grams were housed in groups of four on a 12-hour light/dark cycle with free access to food and water. Test compounds were administered twice daily via i.p. injection, 1 hour before the dark cycle and 2 hours after lights on, for three days. All rats were weighed daily after each morning injection. Overall results were expressed as body weight (grams) gained per day (mean  $\pm$  SEM) and were analyzed by two-way ANOVA. Data for each time point were analyzed by one-way ANOVA followed by post hoc Newman-Keuls test. The data were analyzed using the GraphPad Prism (v2.01) (GraphPad Software, Inc., San Diego, CA). All data were presented as means  $\pm$  S.E.M.

30

Effects of MCH1 Antagonists on Consumption  
of Sweetened Condensed Milk

5 Male C57BL/6 mice (Charles River) weighing 17-19 grams  
at the start of experiments were housed in groups of  
four or five on a 12 hour light/dark cycle with free  
access to food and water. For 7 days, mice were weighed,  
placed in individual cages and allowed to drink  
10 sweetened condensed milk (Nestle, diluted 1:3 with  
water) for 1 hour, 2-4 hours into the light cycle. The  
amount of milk consumed was determined by weighing the  
milk bottle before and after each drinking bout. On the  
test day, mice received i.p. injections of Test Compound  
(3, 10 or 30 mg/kg in 0.01 % lactic acid), vehicle (0.01  
15 % lactic acid) or d-fenfluramine (10 mg/kg in 0.01 %  
lactic acid) 30 min. prior to exposure to milk. The  
amount of milk consumed on the test day (in mls milk/ kg  
body weight) was compared to the baseline consumption  
for each mouse determined on the previous 2 days. Data  
20 for each time point were analyzed by one-way ANOVA.

Forced Swim Test (FST) in the Rat

Animals

25 Male Sprague-Dawley rats (Taconic Farms, NY) were used  
in all experiments. Rats were housed 5 per cage and  
maintained on a 12:12-h light-dark cycle. Rats were  
handled for 1 minutes each day for 4 days prior to  
behavioral testing.

30

### Drug Administration

Animals were randomly assigned to receive a single i.p. administration of vehicle (2.5% EtOH / 2.5% Tween-80), imipramine (positive control; 60 mg/kg), or Test Compound 60 minutes before the start of the 5 minute test period. All injections were given using 1 cc tuberculin syringe with 26 3/8 gauge needles (Becton-Dickinson, VWR Scientific, Bridgeport, NJ). The volume of injection was 1 ml/kg.

10

### Experimental Design

The procedure used in this study was similar to that previously described (Porsolt, et al., 1978), except the water depth was 31 cm in this procedure. The greater depth in this test prevents the rats from supporting themselves by touching the bottom of the cylinder with their feet. Swim sessions were conducted by placing rats in individual plexiglass cylinders (46 cm tall x 20 cm in diameter) containing 23-25°C water 31 cm deep. Swim tests were conducted always between 900 and 1700 hours and consisted of an initial 15-min conditioning test followed 24h later by a 5-minute test. Drug treatments were administered 60 minutes before the 5-minute test period. Following all swim sessions, rats were removed from the cylinders, dried with paper towels and placed in a heated cage for 15 minutes and returned to their home cages. All test sessions were videotaped using a color video camera and recorded for scoring later.

**Behavioral Scoring**

The rat's behavior was rated at 5-second intervals during the 5-minute test by a single individual, who was blind to the treatment condition. Scored behaviors were:

1. Immobility- rat remains floating in the water without struggling and was only making those movements necessary to keep its head above water;
2. Climbing - rat was making active movements with its forepaws in and out of the water, usually directed against the walls;
3. Swimming - rat was making active swimming motions, more than necessary to merely maintain its head above water, e.g. moving around in the cylinder; and
4. Diving - entire body of the rat was submerged.

**Data Analysis**

- The forced swim test data (immobility, swimming, climbing, diving) were subjected to a randomized, one-way ANOVA and post hoc tests conducted using the Newman-Keuls test. The data were analyzed using the GraphPad Prism (v2.01) (GraphPad Software, Inc., San Diego, CA).
- All data were presented as means  $\pm$  S.E.M. All data were presented as means  $\pm$  S.E.M.

**Forced Swim Test (FST) in the Mouse****Animals**

- DBA/2 mice (Taconic Farms, NY) were used in all experiments. Animals were housed 5 per cage in a controlled environment under a 12:12 hour light:dark cycle. Animals were handled 1 min each day for 4 days

prior to the experiment. This procedure included a mock gavage with a 1.5 inch feeding tube.

#### Drug Administration

5     Animals were randomly assigned to receive a single administration of vehicle (5% EtOH/5% Tween-80), Test Compound, or imipramine (60 mg/kg) by oral gavage 1 hour before the swim test.

#### 10     Experimental Design

The procedure for the forced swim test in the mouse was similar to that described above for the rat, with some modifications. The cylinder used for the test was a 1-liter beaker (10.5cm diameter X 15 cm height) fill to 15     800ml (10cm depth) of 23-25°C water. Only one 5-minute swim test was conducted for each mouse, between 1300 and 1700 hours. Drug treatments were administered 30-60 minutes before the 5-minute test period. Following all swim sessions, mice were removed from the cylinders, 20     dried with paper towels and placed in a heated cage for 15 minutes. All test sessions were videotaped using a Sony color video camera and recorder for scoring later.

#### Behavioral Scoring

25     The behavior during minutes 2-5 of the test was played back on a TV monitor and scored by the investigator. The total time spent immobile (animal floating with only minimal movements to remain afloat) and mobile (swimming and movements beyond those required to remain afloat) 30     were recorded.



### Data Analysis

The forced swim test data (time exhibiting immobility, mobility; seconds) were subjected to a randomized, one-way ANOVA and post hoc tests conducted using the Newman-Keuls test. The data were analyzed using the GraphPad Prism (v2.01) (GraphPad Software, Inc., San Diego, CA). All data were presented as means  $\pm$  S.E.M.

### Social Interaction Test (SIT)

Rats are allowed to acclimate to the animal care facility for 5 days and are housed singly for 5 days prior to testing. Animals are handled for 5 minutes per day. The design and procedure for the Social Interaction Test is carried out as previously described by Kennett, et al. (1997). On the test day, weight matched pairs of rats ( $\pm$  5%), unfamiliar to each other, are given identical treatments and returned to their-home cages. Animals are randomly divided into 5 treatment groups, with 5 pairs per group, and are given one of the following i.p. treatments: Test Compound (10, 30 or 100 mg/kg), vehicle (1 ml/kg) or chlordiazepoxide (5 mg/kg). Dosing is 1 hour prior to testing. Rats are subsequently placed in a white perspex test box or arena (54 x 37 x 26 cm), whose floor is divided up into 24 equal squares, for 15 minutes. An air conditioner is used to generate background noise and to keep the room at approximately 74°F. All sessions are videotaped using a JVC camcorder (model GR-SZ1, Elmwood Park, NJ) with either TDK (HG ultimate brand) or Sony 30 minute videocassettes. All sessions are conducted between 1300 - 1630 hours. Active social interaction, defined as grooming, sniffing, biting, boxing, wrestling, following and crawling over or under, is scored using a stopwatch

(Sportsline model no. 226, 1/100

sec.

discriminability). The number of episodes of rearing (animal completely raises up its body on its hind limbs), grooming (licking, biting, scratching of body), and face washing (i.e. hands are moved repeatedly over face), and number of squares crossed are scored. Passive social interaction (animals are lying beside or on top of each other) is not scored. All behaviors are assessed later by an observer who is blind as to the treatment of each pair. At the end of each test, the box is thoroughly wiped with moistened paper towels.

### Animals

Male albino Sprague-Dawley rats (Taconic Farms, NY) are housed in pairs under a 12 hr light dark cycle (lights on at 0700 hrs.) with free access to food and water.

### Drug Administration

Test Compound is dissolved in either 100% DMSO or 5% lactic acid, v/v (Sigma Chemical Co., St. Louis, MO). Chlordiazepoxide (Sigma Chemical Co., St. Louis, MO) is dissolved in double distilled water. The vehicle consists of 50% DMSO (v/v) or 100% dimethylacetamide (DMA). All drug solutions are made up 10 minutes prior to injection and the solutions are discarded at the end of the test day. The volume of drug solution administered is 1 ml/kg.

### Data Analysis

The social interaction data (time interacting, rearing and squares crossed) are subjected to a randomized, one-way ANOVA and post hoc tests conducted using the

Student-Newman-Keuls test. The data are subjected to a test of normality (Shapiro-Wilk test). The data are analyzed using the GBSTAT program, version 6.5 (Dynamics Microsystems, Inc., Silver Spring, MD, 1997).

5

### In Vivo Models of the Micturition Reflex

The effects of compounds on the micturition reflex were assessed in the "distension-induced rhythmic contraction" (DIRC), as described in previous publications (e.g. Maggi et al, 1987; Morikawa et al, 1992), and Continuous Slow Transvesicular Infusion (CSTI) models in rats.

#### 15 DIRC Model

Female Sprague Dawley rats weighing approximately 300 g were anesthetized with subcutaneous urethane (1.2 g/kg). The trachea was cannulated with PE240 tubing to provide a clear airway throughout the experiment. A midline abdominal incision was made and the left and right ureters were isolated. The ureters were ligated distally (to prevent escape of fluids from the bladder) and cannulated proximally with PE10 tubing. The incision was closed using 4-0 silk sutures, leaving the PE10 lines routed to the exterior for the elimination of urine. The bladder was canulated via the transurethral route using PE50 tubing inserted 2.5 cm beyond the urethral opening. This cannula was secured to the tail using tape and connected to a pressure transducer. To prevent leakage from the bladder, the cannula was tied tightly to the exterior urethral opening using 4-0 silk.

To initiate the micturition reflex, the bladder was first emptied by applying pressure to the lower abdomen, and then filled with normal saline in 100 increments (maximum = 2 ml) until spontaneous bladder  
5 contractions occurred (typically 20-40 mmHg at a rate of one contraction every 2 to 3 minutes. Once a regular rhythm was established, vehicle (saline) or Test Compounds were administered i.v. or i.p. to explore their effects on bladder activity. The 5-HT<sub>1A</sub> antagonist  
10 WAY-100635 was given as a positive control. Data were expressed as contraction interval (in seconds) before drug application (basal), or after the application of vehicle or test article.

15 **Continuous Slow Transvesicular Infusion (CSTI) rat Model**

Male Sprague Dawley rats weighing approximately 300 g were used for the study. Rats were anaesthetized with pentobarbitone sodium (50 mg/kg, i.p). Through a median  
20 abdominal incision, bladder was exposed and a polyethylene cannula (PE 50) was introduced into the bladder through a small cut on the dome of the bladder and the cannula was secured with a purse string suture. The other end of the cannula was exteriorized  
25 subcutaneously at the dorsal neck area. Similarly, another cannula (PE 50) was introduced into the stomach through a paramedian abdominal incision with the free end exteriorized subcutaneously to the neck region. The surgical wounds were closed with silk 4-0 suture and the  
30 animal was allowed to recover with appropriate post surgical care. On the following day, the animal was placed in a rat restrainer. The open end of the bladder-cannula was connected to a pressure transducer as well

as infusion pump through a three-way stopcock. The bladder voiding cycles were initiated by continuous infusion of normal saline at the rate of 100  $\mu$ l/min. The repetitive voiding contractions were recorded on a Power  
5 Lab on-line data acquisition software. After recording the basal voiding pattern for an hour, the test drug or vehicle was administered directly into stomach through the intragastric catheter and the voiding cycles were monitored for 5 hours. Micturition pressure and  
10 frequency were calculated before and after the treatment (at every 30 min interval) for each animal. Bladder capacity was calculated from the micturition frequency, based on the constant infusion of 100ul/min. The effect of the test drug was expressed as a percentage of basal,  
15 pre-drug bladder capacity. WAY 100635 was used as positive control for comparison.

In Vivo Results

Table 2

5 Effect of MCH1 antagonist (Example No.) in the following  
 in vivo models: 3-day Body Weight (3D BW), mouse  
 Sweetened Condensed Milk (mSwCM), mouse Forced Swim Test  
 (mFST), rat Forced Swim Test (rFST), DIRC model, or CSTI  
 model.

10

Example No.	3D BW	mSwCM	mFST	rFST	DIRC	CSTI
2	A	B	C	D	E	F
10	Not Done	Not Done	C	Not Done	E	F
39	A	B	Not Done	D	Not Done	Not Done
43	Not Done	B	C	Not Done	Not Done	Not Done
44	Not Done	Not Done	No effect	Not Done	Not Done	Not Done
89	Not Done	B	No effect	Not Done	Not Done	Not Done
90	Not Done	No effect	No effect	Not Done	Not Done	Not Done
91	Not Done	Not Done	C	Not Done	E	F
93	Not Done	Not Done	No effect	Not Done	Not Done	Not Done
95	Not Done	B	No effect	Not Done	Not Done	Not Done
99	A	Not Done	C	Not Done	E	F
105	Not Done	B	C	Not Done	Not Done	Not Done
106	Not Done	B	C	Not Done	E	F
112	Not Done	Not Done	No effect	Not Done	Not Done	Not Done
116	A	Not Done	C	Not Done	E	F

15

A = Produced a significant reduction in weight gain relative to vehicle-treated controls

- 5      B = Produced a significant decrease in  
consumption of milk relative to vehicle-  
treated controls
- C = Produced a significant decrease in immobility  
relative to vehicle-treated animals when  
administered orally.
- D = Produced a significant decrease in immobility  
or a significant increase in swimming activity  
relative to vehicle-treated animals
- 10     E = Produced a significant increase in contraction  
interval relative to pre-drug interval
- F = Produced an increase in bladder capacity in  
rats relative to baseline capacity.
- 15

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